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SURGERY

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SURGERY

VOL. 35 FEBRUARY, 1954 No. 2

Original Communications

PRIMARY CARCINOMA OF THE LUNG

RESULTS OF SURGICAL TREATMENT

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THE aim of this work is to present the results of our experience with the surgical treatment of bronchiogenic carcinoma. It is based upon a series of 800 cases from our hospital and private practice; 311 were operated upon and in 200 a resection was done.

TABLE I. OPERABILITY (1944 TO 1952)

Number of patients observed	880
Number of patients resected	200
Operative index	22.7%

This figure is not quite right in absolute terms, because our cases are surgical and therefore represent a selection; but it is useful for comparative purposes. The operative index depends on the criteria of extension of resection in advanced cases and, mainly, of palliative resections when they are performed. We advocate wide resections in advanced cases and palliative operations only when during thoracotomy the propagation precludes radical resection; in other words, we do not perform deliberate palliative resections.

In 1948,[1] we stated that by taking advantage of all favorable circumstances operability could reach 50 per cent, which is a substantial proportion.

In our series the operative index has increased in these percentages:

1947	13.1 per cent
1949	17.6 per cent
1952	22.7 per cent

It is lower than Ochsner and associates'[2] figures, 35 per cent (1952), but near Churchill and co-workers',[3] 25.1 per cent (1950). Edwards[4] (1946) could resect in only 70 cases out of 1,016, scarcely 7 per cent.

Read before the Inter-American Congress of the American College of Surgeons, São Paulo, Brazil, Feb. 11, 1953.

Received for publication, April 6, 1953.

*Assistant Professor, Thoracic Surgery, University of Buenos Aires Medical School.

TABLE II. RESECTABILITY

Number of patients explored	311
Number of patients resected	200
Resectability index	64.3%

Resectability index reveals the accuracy of operability diagnosis and of handling of advanced cases, in other words, the ability to decide whether a case is resectable or not. It increases with the accuracy of the detection of extension indicating inoperability and with the use of new techniques of radical resection.

In our series the resectability was:

1947	40.7 per cent
1949	56.0 per cent
1952	64.3 per cent

Ochsner's[2] figure is 64.8 per cent and Churchill's[3] 58.0 per cent.

TABLE III. MORTALITY (1944 TO 1952)

Number of patients resected	200
Number of deaths	37
Gross mortality	18.5%

Thirty-seven patients died immediately or several weeks after operation (18.5 per cent). In order to evaluate the risk of operation we must consider the time the operation was performed, because in later years surgical skill has become greater and antibiotics and a better understanding of prevention of shock have been available. Furthermore, it is essential to consider the extent of resection and, finally, whether the patient is in a private or charity hospital must be considered.

Our series comprises only one period (1944 to 1952).

TABLE IV. MORTALITY AND INFLUENCE OF THE TYPE OF OPERATION

TYPE OF OPERATION	NUMBER OF CASES	DEATHS	PER CENT
Pneumonectomy	159	35	22.0
Lobectomy	41	2	4.8

Most deaths occurred in the pneumonectomy group, partly because of the greater risk, but chiefly because lesions so treated were more extensive and propagated to the mediastinum as demonstrated by these figures:

	Number of Cases	Deaths	Per Cent
Atypical resections	119	31	26.0
Typical resections	81	6	7.4

We consider reaction atypical when it is carried beyond the borders of the organ, thus altering the standard technique. Details are given in the following figures.

	Number of Cases	Deaths	Per Cent
Mediastinal dissection	33	4	12.1
Parietal and mediastinal dissection	6	2	33.3
Intrapericardiac maneuvers	4	1	25.0
Suture of the auricle	4	2	50.0
Block resection of chest wall	9	6	66.6

TABLE V. MORTALITY AND INFLUENCE OF TYPE OF HOSPITAL

TYPE OF HOSPITAL	NUMBER OF CASES	DEATHS	PER CENT
Charity hospital	104	28	26.9
Private practice	96	9	9.3

Such a remarkable difference depends on the type of patients treated, in that the charity patient generally has a more advanced lesion; also, in private clinics there is better nursing and medical care.

Operation	Hospital	Number of Cases	Deaths	Per Cent
Pneumonectomy	Charity hospital	91	27	29.6
	Private practice	68	8	11.7
Lobectomy	Charity hospital	13	1	7.5
	Private practice	28	1	3.5

In both institutions the mortality in the lobectomy series was low, a consequence of the fewer nursing requirements. Lobectomy was twice as common in private practice as in charity patients, an index confirming the theory that the more favorable cases are predominately those of private patients. Conversely, in the charity series, pneumonectomy, with its higher mortality, was performed more often because the lesions are more advanced.

From the foregoing it is evident that the mortality increases with the extent of the lesion and the type of operation.

We cannot change the extent of the resection except by early diagnosis, which is dependent upon education of the medical profession concerning the frequency of bronchiogenic carcinoma. The extent of resection, which depends on the extent of the growth, rests on a choice between lobectomy and pneumonectomy. In certain cases, with small, peripheral tumors, without glands and with free fissures, we prefer lobectomy because we consider the operation as radical or as palliative as pneumonectomy, with the advantage of its low operative mortality and better functional prognosis. The feasibility of this procedure is still open to question and because of this we cite our results. We do not believe that there is a place for standards in the treatment of a disease such as cancer where we cannot warrant any cure and where we proceed only under the guidance of the gross findings provided by clinical investigation.

Of 200 patients submitted to resection 37 died shortly after operation and, excluding 13 others not traced, there remained 150. Ninety-two of them died postoperatively from recurrence and other causes; 58 are still alive.

Most of the postoperative deaths occurred within two years, the so-called "critical" period. The patients who survive this period without signs of recurrence have a good chance of cure.

TABLE VI. SURVIVALS

	Of 92 Patients Who Died		
Critical period	0 to 6 months	32	81
	6 months to 1 year	31	
	1 to 2 years	18	
	2 to 3 years	8	
	3 to 4 years	3	
	Of 58 Patients Still Alive		
	6 months to 1 year	13	
	1 to 2 years	11	
Over 2 years	2 to 3 years	11	34
	3 to 4 years	8	
	4 to 5 years	8	
	More than 5 years	7	

It is interesting to study the survival rate in relation to the type of resection and to the characteristics of the tumor (histology and spread).

TABLE VII. SURVIVALS OVER TWO YEARS IN RELATION TO TYPE OF RESECTION

TYPE OF OPERATION	NUMBER OF OPERATIONS	NUMBER OF SURVIVALS	PER CENT
Pneumonectomy	104	25	24.0
Lobectomy	21	9	42.8
Total	125	34	27.2

Concerning long-time survivals we can consider only pneumonectomy and lobectomy, as we have not had enough experience with the radical resections because of the small number of such operations performed and the short period of time which has elapsed (under two years). Excluding thirteen cases not traced, 125 resections were performed between 1946 and 1950, with a minimum of two years' postoperative course. Thirty-four patients are still alive (27.2 per cent), a figure very similar to those obtained by Churchill and Ochsner and inferior only to Taylor and associate's.[5] We surmise that our five-year survival rate might be similar to Ochsner's and we believe that the cure rate following surgical treatment of bronchiogenic carcinoma should be 25 per cent.

But the most interesting feature is the comparative study of lobectomy and pneumonectomy to establish their respective curative value. The overall figure is very impressive: 42.8 per cent for lobectomy against 24.0 per cent for the pneumonectomy series. Churchill reports the same results: lobectomy 26 per cent and pneumonectomy 22 per cent survival rate after five years. In Churchill's series the operative mortality was not a significant factor because it was more or less the same for both operations; in our cases mortality was quite different in the two series, thus explaining the great difference between the respective figures.

We do not assume that lobectomy is a more radical operation than pneumonectomy because we know that the tumors treated by partial resection have a better prognosis, but this fact confirms the idea that in selective cases the radicality of the two is equivalent. Therefore, it is advisable not to lose the opportunity to perform a lobectomy with its accompanying advantages, low mortality and excellent immediate and functional results.

TABLE VIII. SURVIVALS. HISTOLOGY AND PROPAGATION OF THE TUMOR

*(A) Histologic classification of 185 resected patients**

TYPE	NUMBER OF CASES	PER CENT
Epidermoid carcinoma	101	55.1
Adenocarcinoma	58	31.3
Undifferentiated	17	9.2
Sarcoma	5	2.7
Alveolar cell tumors	2	1.0
Endothelioma	2	1.0

*Ten cases of bronchial adenoma are not included.

(B) Histologic classification and propagation of 33 resected patients who survived more than two years

TYPE	WITHOUT PROPAGATION	WITH PROPAGATION	TOTAL	PER CENT
Epidermoid	18	2	20	60.6
Adenocarcinoma	11	1	12	36.3
Sarcoma	1	–	1	–
Total	30	3 (9%)	33	–

(C) Histologic classification and propagation of 9 lobectomy patients who survived more than two years

TYPE	WITHOUT	WITH
Epidermoid	3	–
Adenocarcinoma	6	–
Total	9	–

(D) Histologic classification and propagation of 24 pneumonectomy patients who survived more than two years

TYPE	WITHOUT	WITH	TOTAL	PER CENT
Epidermoid	15	2	17	70.8
Adenocarcinoma	5	1	6	25.0
Sarcoma	1	–	1	4.2
Total	21	3	24	–

Of 200 resected cases 15 were not well classified but the remainder, 185, were. Epidermoid carcinoma constituted the majority with 55.1 per cent, followed by adenocarcinoma with 31.3 per cent and undifferentiated 9.2 per cent. These figures are different from those obtained in the pathologic laboratories in which there is a higher proportion of the last grouping. It is recognized that this disparity lies in the smaller degree of malignancy of the epidermoid and adenocarcinoma which offer a greater chance for surgical treatment.

The respective malignancies of these lesions in patients surviving two years is demonstrated in Table VIII, (*b*).

Epidermoid carcinoma was present in 60.6 per cent and adenocarcinoma in 36.3 per cent. Most tumors had no metastases (thirty of thirty-three); only three of the patients, or 9 per cent, who are still alive had metastases. The bad prognosis of carcinoma with lymphatic propagation has been stressed by Ochsner, who considers resection palliative under these circumstances. Although Graham does not subscribe to this opinion, it is prevalent. The poor results obtained in cases with metastases have prompted many surgeons to perform more extensive resections with dissection of the lymphatics of the mediastinum.

It is interesting to consider the relationship of the type of tumor and the type of operation in the patients who survived more than two years [Table VIII, (*c*) and (*d*)]. In the lobectomy group adenocarcinoma was the more prevalent whereas the reverse was true in epidermoid carcinoma. The explanation lies in the fact that adenocarcinoma constitutes most of the peripheral tumors without lymphatic spread which makes lobectomy feasible. In our series many were asymptomatic and were revealed only occasionally by a rheumatoid syndrome of the Bamberger-Marie type. The malignancy of these tumors is not higher than the malignancy of the epidermoid cancers but they have a longer development with a prolonged asymptomatic period.

In the pneumonectomy group, epidermoid carcinomas comprise 70.8 per cent of the cases because of the common localization of these tumors in the hilum of one lung and because of early lymphatic spread which makes it imperative to resect the entire lung.

From the preceding study of the relationships between survivals and the type of excision and the characteristics of the tumor, it is evident that the chief factor in prognosis lies in the extension of the tumor and its actual propagation; the second important factor is histologic type. Conversely, survival is independent of the type of resection. This means that prognosis does not depend as much on histology and extent of resection as on extension of the disease.

SUMMARY AND CONCLUSIONS

1. The operability rate in our series of 880 cases of bronchiogenic carcinoma with 200 resections is 22.7 per cent; it has increased through the years and could reach 50 per cent.

2. Resectability index on 311 thoracotomy cases with 200 resections is 64.3 per cent; it is still increasing, although not as much, because of accuracy of preoperative diagnosis and because of the new field opened by wide resections. There will always be a margin for the exploratory thoracotomy which must not be restricted.

3. Over-all operative mortality is 18.5 per cent. In the pneumonectomy series it was 22 per cent and in lobectomy it was 4.8 per cent. In typical operation, mortality descends to 7.4 per cent, whereas, in atypical operation, it ascends to 26 per cent. The greater risks are in block resections of the chest wall, in patients with suture of the auricle, in combined parietal mediastinal dissection, and in intrapericardial maneuvers. Conversely, mediastinal dissection alone does not add any extra risk. The mortality varies with the type of hospital, 26.9 per cent in charity hospitals and 9.3 per cent in private clinics. This can be explained by major extension and seriousness of disease in charity patients and the better nursing provided by private clinics.

4. Over-all survival includes fifty-eight cases; thirty-four of the patients are living more than two years after the operation, the so-called critical period of recurrences. This represents a 27.2 per cent late-survival rate.

5. Studying the survivals after two years according to the type of resection, it is apparent that lobectomy has advantages over pneumonectomy

because of the different kinds of tumors submitted to each procedure. But at least it is apparent that this operation is as radical as pneumonectomy when strictly circumscribed as to its indications and contraindications.

6. When the relationship between survivals and histology of the tumor is considered, it appears that there is a great prevalence of epidermoid carcinoma in the resected group and that increases in the two-year-survival series are undoubtedly an index of lower malignancy. Late survival in propagated cases was very small, 9 per cent, confirming the opinion that resection in such cases is mostly palliative. This finding is mandatory for more extensive resections, the so-called radicals, with dissection of mediastinal glands.

7. The lobectomy series, which includes less advanced and nonpropagated tumors, shows a sharp predominance of the adenocarcinoma type; this means that its malignancy does not exceed that of the epidermoid group, according to its evolutive degree.

8. General conclusions regarding mortality and survival are:

(a) Operative risk rises with extension of lesions and width of excision.

(b) Prognosis is less dependent on the histologic type of the growth and extension of the excision than it is related to propagation of the disease.

(c) The philosophy of doctors dealing with this problem must be to concentrate their efforts on trying to detect cases earlier than on devising wider operations.

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SHOCK AND THE ADRENOCORTEX

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SHOCK is a syndrome resulting from depression of many functions, but in which reductions of the effective circulating blood volume and of the blood pressure are of basic importance, and in which impairment of the circulation steadily progresses until it eventuates in a state of irreversible circulatory failure.[25] In any consideration of the shock problem it is necessary to differentiate between the factors which initiate and those which perpetuate the syndrome. The favorable effects of blood-replacement therapy have served to focus attention on the reduction in the effective blood volume and its immediate circulatory consequences to the neglect of other factors. In the past, the concept of decreased effective circulating volume seemed adequate to explain the initiation and the early manifestations of the shock syndrome, such as hypotension and vasoconstriction; it shed no light, however, on either the nature of the compensatory mechanisms involved or the reason for their deterioration as the shock syndrome progressed.

Shorr and his associates, studying the pathophysiology of the terminal vascular bed, provided a clear analysis of the striking contrasts that exist when shock is reversible and when it is irreversible.[19-22] By direct visualization of the peripheral blood vessels in the mesentery, they were able to distinguish two consecutive stages in the shock syndrome. The initial compensatory phase apparently was related to a reduction in blood volume; the decompensatory phase was related to the period of inadequate peripheral blood flow. The compensatory response was characterized by a hyperreactive condition of the peripheral blood vessels, as evidenced by an increasingly enhanced reactivity of the terminal muscular vessels to epinephrine and an increase in the spontaneous vasomotor movements of the smallest arterioles and precapillaries. This type of heightened reactivity persisted even when the blood loss was acute and sufficient to precipitate the collapse of the animal. The resultant capillary ischemia and the restriction of peripheral blood flow into the most direct thoroughfare channels served to maintain an active venous return of blood from the tissues until shortly before death.

On the contrary, with the development of an irreversible type of shock following prolonged hypotension, a new set of vascular changes progressively appeared and disrupted the peripheral circulation. These changes were decompensatory in nature and initially were made evident by a progressive

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decrease in epinephrine reactivity and a slowing and, finally, complete cessation of spontaneous vasomotor caliber changes in the terminal arterioles. The loss of these compensatory influences on the peripheral circulation resulted in the diversion of increasing amounts of blood into the capillary side channels, from which it failed to return to the active circulation. This, in turn, led to the

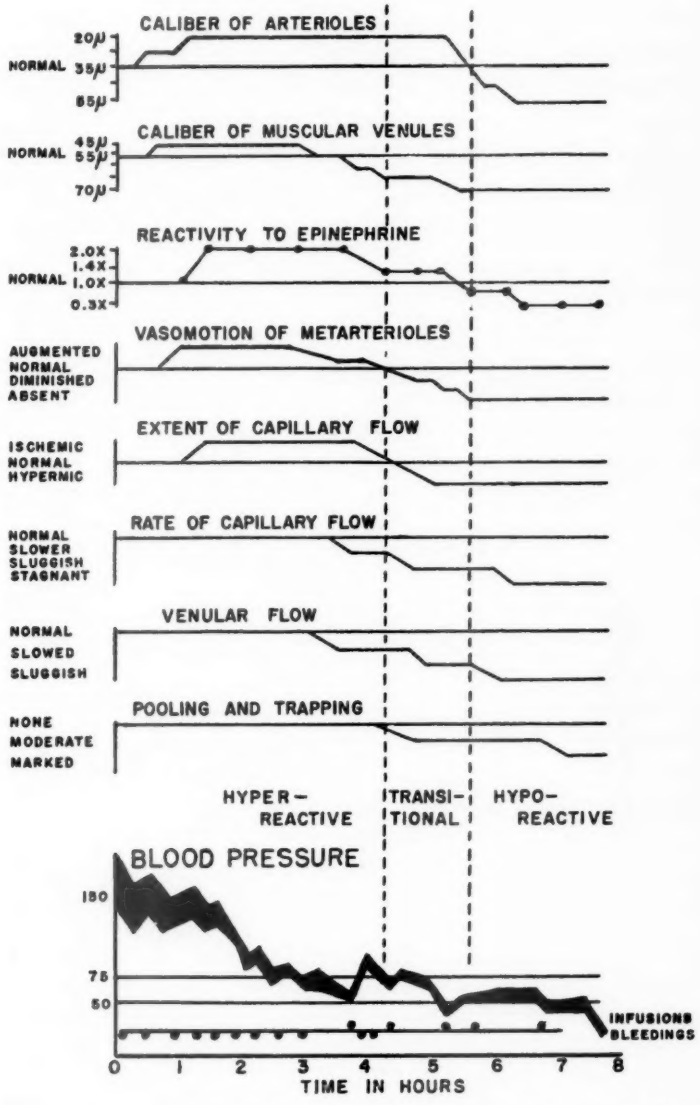


Fig. 1.—Graphic presentation of observations made during shock on the terminal vascular bed contrasting the findings in the hyperreactive or reversible phase and the hyporeactive or irreversible phase of shock. Note the beneficial results on blood pressure from a reinfusion of blood during the reversible state and the failure to improve the hypotension by repeated transfusions in the irreversible state. (From Zweifach.[26])

eventual failure of venous return and to peripheral circulatory collapse. Once this hyporeactive stage had fully developed, transfusions exerted only a transient, if any, benefical effect, a state of irreversibility to replacement therapy having been reached (Fig. 1).[26] In simple contrast, referable to the

terminal vascular bed, then, reversible shock is characterized by augmented vasomotion, accentuated response to epinephrine, ischemic capillary blood flow, and slowed venular flow. Irreversible shock is characterized by absent vasomotion, no response to epinephrine, over-all capillary blood flow, and stagnant venular return. In the latter condition, transfused blood is trapped in the stagnant pool of the capacious capillary bed, and results in no improvement in the over-all hemodynamic response.

The immediate readjustments leading to vasoconstriction following hemorrhage are such that an insight into one of the mechanisms perpetuating a shock state may be apparent.[28] Subsequent to a functional reduction in circulating blood volume, there is decreased filling of the right side of the heart and reduced cardiac output. A natural consequence of decreased cardiac output is a fall in blood pressure in the aorta and arteries. As a measure of visceral blood flow, these findings should be correlated with the demonstrated decrease in renal plasma flow,[4, 13, 18] the reduction being greater than the fall in blood pressure, indicating increased renal resistance or vasoconstriction.[11] There is, thus, a decreased minute volume of blood delivered to the kidney and, presumably, to the adrenal gland, with a subsequent possible reduction in the amounts of adrenocortical steroids available in the circulation per unit time for peripheral tissue utilization. This is particularly true as the peripheral vascular bed in general, as well as the vascular bed of the adrenocortex, undergo the changes coincident with the development of irreversible shock. Zweifach,[27] moreover, has reported that the absence of the adrenocortex blunts the adequacy of the compensatory mechanisms in reversible shock and that adrenocortical steroids will restore terminal vascular epinephrine responsivity in decompensated or irreversible shock.

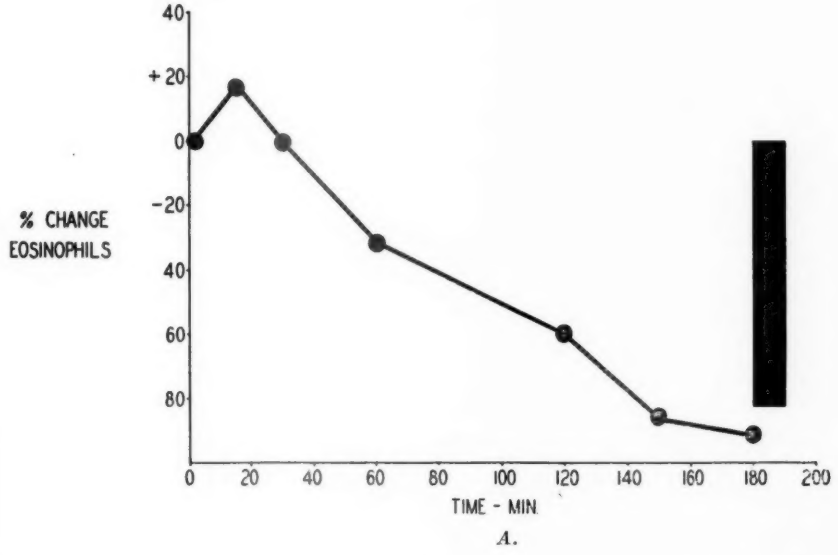
A clinical evaluation of shock occurring in patients who possess an unrecognizedly limited or borderline adrenocortical reserve and of shock in patients who presumably are endocrinologically normal, but who do not respond to blood replacement therapy, seems to be of interest.

Among other changes, it has been well established that the circulating blood level of the C-11, 17-oxygenated adrenocortical steroids is reflected by the number of eosinophils circulating in the blood stream.[3, 5, 8] In man, failure to demonstrate an eosinopenia following the administration of adrenocorticotropic hormone should be considered evidence of adrenocortical insufficiency;[23] if eosinopenia does not follow operation, failure of the adrenocortex should be suspected.[16] Even though many objections have been raised as to the suitability of this measure of adrenocortical activity, it still remains, recognizing its limitations, the simplest and quickest evaluation of adrenocortical function. The demonstration of a high eosinophil count at a time when past experiences indicate it should be low is substantiative evidence of an inadequate supply of adrenocortical steroids.

MATERIALS AND METHODS

The first part of this study demonstrates different patterns of endocrine response in known normal and known abnormal endocrinologic patients. Some of the patients described in this part of the study have been reported

previously.[6] Nearly all the patients studied were subjected preoperatively or pretreatment to either the epinephrine-eosinophil response or the ACTH-eosinophil response (Thorn) test, or both. In the former, the test dose of epinephrine was 0.3 c.c. of a 1:1,000 dilution injected subcutaneously. In the latter, the test dose was 25 mg. of ACTH injected intramuscularly. Examinations were made in the postabsorptive state, and the control eosinophil count was taken immediately preceding, and the second count exactly four hours after, the injection of the test material. The cell counts were made in a Levy chamber according to the method recommended by Randolph and Rollins.[14] For the study made during the operative procedure, a control count was taken prior to the induction of anesthesia, and serial counts were made during the course of the operation. The counts were recorded as percentage changes from the control counts in the endocrinologically normal cases and from the pretreatment counts in the adrenocortical-deficient patients. The patients in this part of the study included: normal patients without operative complications, a normal patient with an operative complication, an adrenocortical-deficient patient without preparation, adrenocortical-deficient patients prepared with cortisone, and an adrenocortical-deficient patient prepared with adrenocorticotropic hormone.



A.

Fig. 2.—Patterns of adrenocortical activity in varying clinical situations depending on severity of stress and type of hormonal preparation as reflected in the eosinophil count.

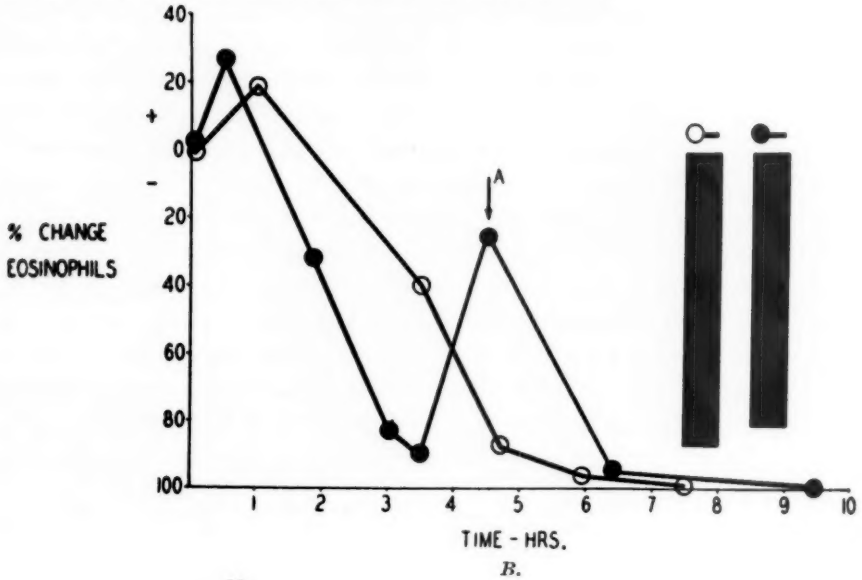
A, Pattern of normal response. Bar graph indicates means eosinophil fall in the normal cases tested preoperatively by the epinephrine-eosinophil response test. The line graph indicates the average pattern of eosinophil fall during the surgical procedure.

The second part of this study deals with case reports of patients in shock treated with adrenocortical extract, cortisone, adrenocorticotropic hormone, or various combinations of these agents.

RESULTS

Employing the circulating eosinophil level as a measure of adrenocortical function, several characteristic patterns of endocrine response during opera-

tive procedures have been obtained (Fig. 2). The type of response depends on the functional integrity of the pituitary-adrenocortical axis, the severity of the stress, and the type of hormone-substitution therapy employed in preparing the deficient patients for operation.



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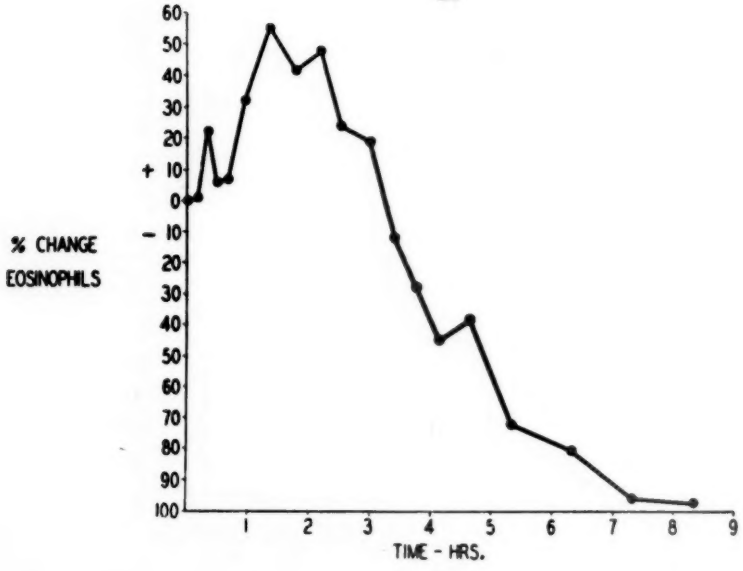


C.

Fig. 2 (*continued*).

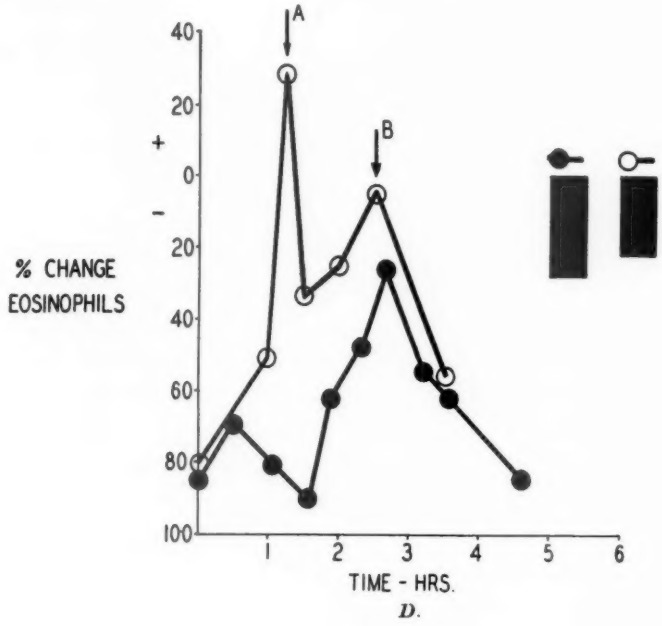
B, Pattern of normal response with a superimposed severe stress. Bar graphs show normal preoperative epinephrine-eosinophil tests. These are comparable cases, but the patient represented by the closed circles had a major hemorrhage as a complication at Point *A*.

C, Pattern of mild adrenocortical insufficiency without preoperative preparation. At two and one-half hours adrenocortical extract was given because of severe shock. [From SURGERY 32: 815 (Nov.) 1952.]

Normal Pattern of Response.—Fig. 2, *A* illustrates mean changes in a group of normal patients. The bar graph indicates a satisfactory response to the epi-

nephrine test as a preoperative evaluation. The line graph demonstrates an initial eosinophilia, then a prompt and rapidly progressive activation of the adrenal cortices early in the course of the operative procedure as reflected in the eosinophil count.

Pattern of Severe Stress Superimposed on a Normal Response.—Fig. 2, *B* compares two patients with the same diagnosis of cardioesophageal carcinoma



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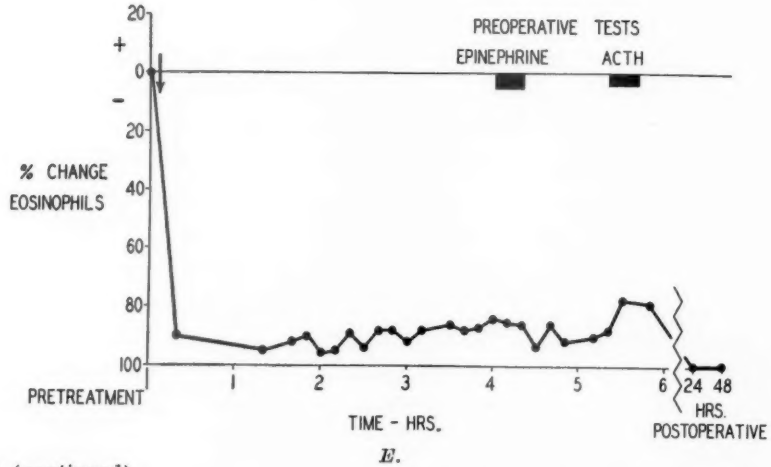


E.

Fig. 2 (*continued*).

D, Pattern of adrenocortical insufficiency in patient prepared for operation with cortisone acetate. The bar graphs are evidence of hypoadrenocorticism. The line graphs compare the minor relative adrenocortical insufficiency of a technically easy operation (closed circles) with the severe insufficiency of a very difficult case (open circles). Both patients required adrenocortical extract during operation. At Points *A* and *B* the patient was without detectable blood pressure but promptly responded to adrenocortical extract in large amounts.

E, Pattern of adrenocortical insufficiency in patient prepared for operation with ACTH. The bar graphs indicate the severe degree of secondary hypoadrenocorticism existing preoperatively. The rate of administration of ACTH during operation was adjusted to the eosinophil counts taken serially throughout the procedure.

subjected to a resection via a thoracoabdominal approach. These patients in all respects were comparable surgical risks and displayed comparable preoperative responses to the epinephrine-eosinophil tests (bar graphs). At Point *A* the patient represented by the closed circles was subjected to a sudden blood loss estimated at 500 c.c. with an immediate rise in eosinophil count and a profound fall in systolic blood pressure to 55 mm. Hg. No drug therapy was given, but overreplacement of 1,500 c.c. of blood was necessary to stabilize the blood pressure and eosinophil count.

Pattern of Mild Adrenocortical Insufficiency Without Hormonal Preparation (Fig. 2, *C*).—This patient had received testosterone propionate 50 mg. daily for one week prior to an exploratory laparotomy of two hours' duration. The preoperative treatment with the androgen had resulted in a progressive loss of the pituitary-adrenocortical response to the same stress of epinephrine. This decreased responsiveness is demonstrated by a change from a 60 per cent fall in eosinophils during the test, prior to the hormone administration, to a 40 per cent fall after hormone administration. This represented a condition of mild pituitary-adrenocortical insufficiency[1, 2] due to a delayed release of pituitary ACTH.[7] During the course of the operative procedure (Fig. 2, *C*), there was strong evidence of adrenocortical insufficiency in the serial eosinophil counts; the operative course was characterized by moderately to severely intractable shock which responded poorly to the continuous use of pressor agents and blood transfusion, although operative blood loss was significantly low. It was necessary at the termination of the operation to give 150 c.c. of aqueous adrenocortical extract, which promptly returned the blood pressure to normal coincidentally with the prompt fall in eosinophils seen after two and one-half hours.

Pattern of Adrenocortical Insufficiency Prepared With Cortisone (Fig. 2, *D*).—The two patients represented in this figure were known to be moderately severe hydroadrenocortical (diagnosis: chromophobe adenoma of the pituitary). The bar graphs indicate the restricted responses to the test dose of epinephrine in each case. Both of these patients were prepared for operation by four daily intramuscular injections of 100 mg. of cortisone acetate. Two hours before operation, each received intramuscular injections of 50 mg. of cortisone acetate at two different sites. The control eosinophil counts just prior to the induction of the anesthesia clearly show that each patient was in a hyperadrenocortical state at that time. Since cortisone acetate has a fixed solubility in tissue fluids, the available synthetic adrenocortical steroid was at a fixed level throughout the operative procedure (craniotomy for optic chiasma decompression). The patient who is represented by the closed circles in Fig. 2, *D* had a primary operation without prior irradiation, which was technically not difficult. In this instance, as evidenced by the rise in the number of eosinophils, temporary very mild adrenocortical insufficiency supervened but was controlled by the prompt administration of aqueous adrenocortical extract. The operative course, as judged from the anesthesia record, was entirely uneventful.

On the other hand, the patient represented by the open circles presented difficulty in management. This was a secondary operation following irradiation and was an extremely difficult procedure technically. It is quite apparent that the degree of adrenocortical insufficiency, as followed by the eosinophil count, was of a much more striking degree. At the points designated *A* and *B*, the patient was without a detectable blood pressure, but the rapid infusion of 100 c.c. of aqueous adrenocortical extract at each instance produced an instantaneous return of blood pressure to 110 mm. Hg. This case presents interesting information concerning the rate of utilization of available adrenocortical hormones (fixed in these cases) as correlated with the severity of the stress and the clinical course; the greater the severity of the stress, the greater is the demand for hormone to effect homeostasis.

Pattern of Adrenocortical Insufficiency Prepared With ACTH (Fig. 2, *E*). —The patient who was the subject of this method of preparation had a recognized case of primary panhypopituitarism with secondary hypoadrenocorticism. Preoperative evaluations by both the epinephrine and ACTH tests are shown by the bar graphs; a very significant degree of hypoadrenocorticism was present. The preoperative preparation consisted of a prolonged course of intramuscular ACTH, to which the metabolic response was sluggish and which required intravenous supplementation (see metabolic data concerning this patient in the Case Reports section of this article).

The patient was carried through the operation (a six-hour pneumonectomy for bronchogenic carcinoma) without adrenocortical extract. A constant intravenous infusion consisting of 40 mg. of ACTH per liter of 5 per cent dextrose in distilled water was maintained. The rate of administration was governed qualitatively by the serial eosinophil counts taken during operation. The course of the surgical procedure as judged by the anesthesia record was completely uneventful. It is of importance to point out how much more physiologic is the control of the patient's response by the varying administration of ACTH, as in this case, than by prior preparation with a fixed level of hormonal activity, as in the preceding cases of patients prepared with cortisone.

CASE REPORTS

CASE 1 (721637).—W. O., a 59-year-old white man, was scheduled for a pneumonectomy for bronchogenic carcinoma. All diagnostic examinations completed prior to operation revealed no stigmata of endocrine dysfunction. Immediately after the induction of anesthesia and the beginning of the skin incision, the patient's blood pressure fell precipitously, and he did not respond adequately to the use of pressor agents or blood transfusion. The operative procedure was discontinued immediately, and the patient was allowed to recover from the anesthesia. No unusual sequelae were apparent. Three days later, on successive days, the patient was tested by the epinephrine and the ACTH tests with remarkably decreased responses (Fig. 2, *E*). Additional examinations made at this time suggested hypogonadism and hypothyroidism. Laboratory examinations revealed a twenty-four hour urinary excretion of pituitary gonadotrophin of 3 M. U. (normal: 6.6 to 53), a serum-protein-bound iodine level of 0.1 gamma per cent, a total serum-cholesterol level of 131 mg. per cent, and a twenty-four hour urinary excretion of 7.6 mg. of 17-ketosteroids. Intravenous pyelograms were normal. The concluded diagnosis was panhypopituitarism with secondary hypoadrenocorticism.

The patient was subsequently placed on a metabolic balance regimen with a constant dietary intake of 125 Gm. of protein (20 Gm. of nitrogen), 350 Gm. of carbohydrate, and total calories of 4,000 per day. This dietary program included 9.3 meq. of sodium and 117.7 meq. of potassium daily. The metabolic data of the entire study are graphically presented according to the method of Reifenstein, Albright, and Wells[15] in Fig. 3. After an equilibration period of six days, intramuscular ACTH therapy was begun at the dosage of 100 mg. per day; the lag in metabolic, eosinophil level and 17-ketosteroid excretion is very apparent and confirms the diagnosis of secondary atrophy of the adrenal cortices. The maximal metabolic responses characteristic of the desired state of hyperadrenocorticism were not attained until an additional daily dose of 10 mg. of ACTH was given intravenously over an eight-hour period. It is noteworthy that water retention was prohibited by the severe sodium restriction and that an additional water load was promptly excreted in the hyperadrenocortical state. At the completion of the metabolic-study period the patient was operated upon under the plan discussed previously, employing ACTH (illustrated in Fig. 2, *E*). The operative course and convalescence were uneventful during the gradual withdrawal of the tropic hormone.

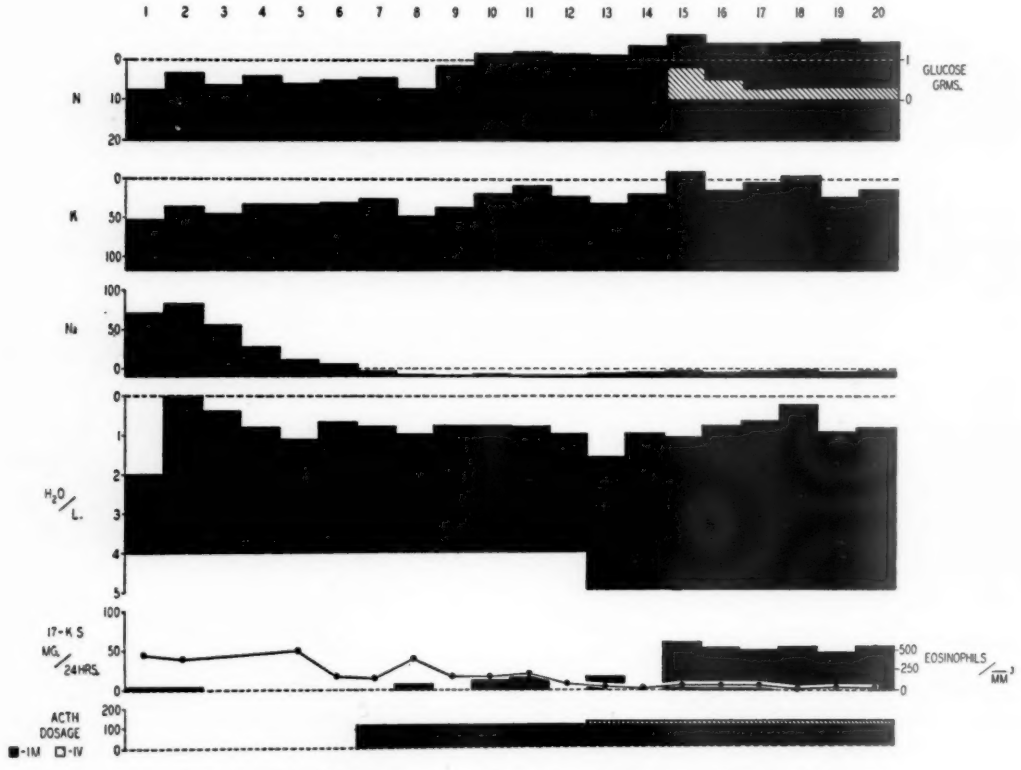


Fig. 3.—Metabolic data on Case 1. (See text for details.)

CASE 2 (B58507).—M. H., a 54-year-old white man, was admitted to the hospital with a diagnosis of a residual pulmonary tuberculous cavity under a thoracoplasty; it was planned to perform a left pneumonectomy. Two preoperative ACTH-eosinophil tests are presented graphically in Fig. 4. It is to be emphasized that the patient presented no laboratory or physical evidence of endocrinologic abnormality. This same illustration shows the preoperative preparation of this patient with cortisone. Fig. 5 demonstrates the essential data from this patient's anesthesia record and shows an essentially stable course during the procedure. It is pertinent that aqueous adrenocortical extract was given intravenously during the operative procedure as the quality of the pulse or the surgeon's clini-

cal evaluation of the cardiac action indicated. Fig. 4 shows the plan of withdrawal of the cortisone in the convalescent period and the rising eosinophil count with the withdrawal. The patient's postoperative period was completely uneventful, and he was discharged on the fifteenth postoperative day.

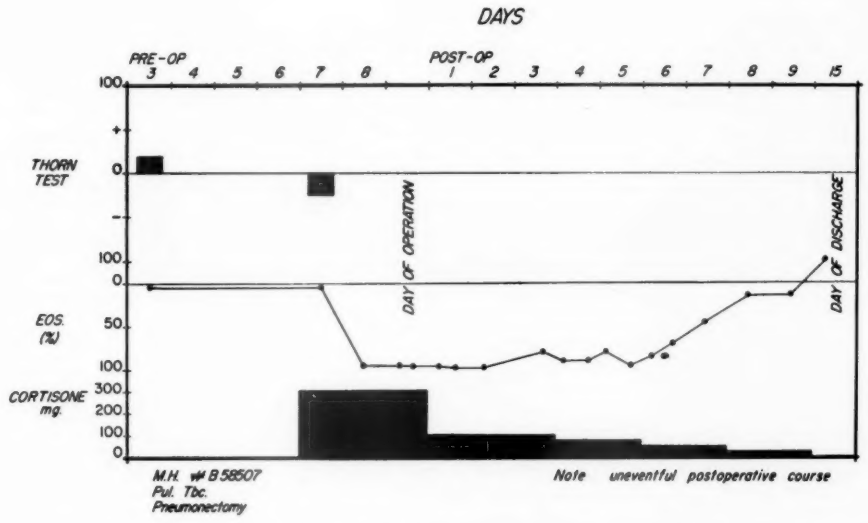


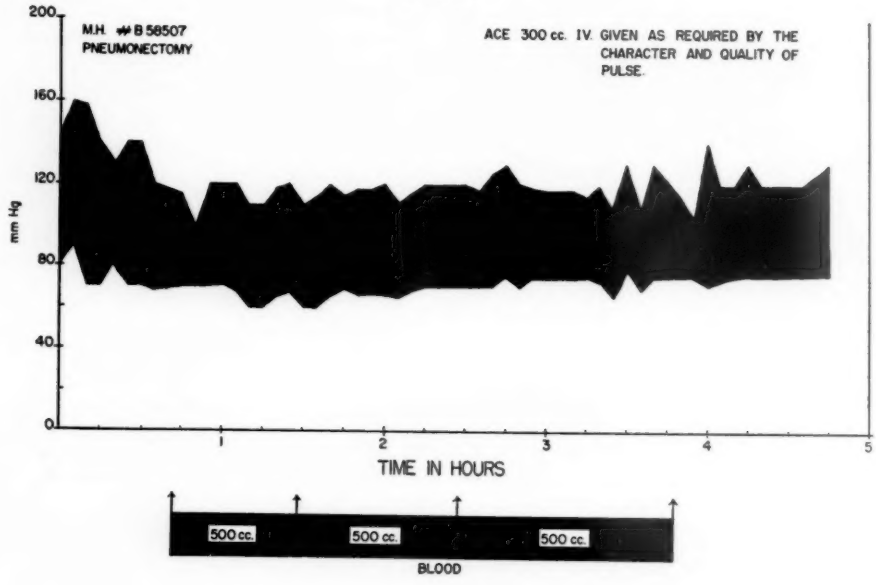
Fig. 4.—Preoperative Thorn tests and essential clinical data on Case 2. (See text for details.)

Case 3 (38-32-07).—M. C., a 65-year-old white woman, was admitted to the hospital with a diagnosis of carcinoma of the gastric cardia involving the lower esophagus. As a result of the concomitant obstruction, the patient was in a state of severe malnutrition. After what was considered satisfactory preparation for operation, resection was accomplished through a thoracoabdominal incision. The operating surgeon had not been correctly informed of the results of the preoperative Thorn test, which had shown only a 27 per cent fall in eosinophils. Fig. 6 illustrates the important data from the anesthesia record. It is readily apparent that the problem of shock was of great significance. Despite the use of pressor agents and a continuous flow of blood, the situation became precarious about two hours after the induction of the anesthesia. The surgeon by this time was committed to completion of the operation. An eosinophil count taken at this time was 334 cells per cubic millimeter, at a time when it should have been approaching 0. Recalculation of the Thorn test data confirmed the diagnosis of adrenocortical insufficiency. The dramatic response to the first intravenous dose of adrenocortical extract is apparent. The prompt responses of the blood pressure and the general condition of the patient to each administration of the extract were impressive. Because of the rapid utilization of the injected hormone,[24] it was practically impossible to maintain a stable state. At the point indicating cortisone administration, 500 mg. of this synthetic steroid was injected intramuscularly at ten different sites, 50 mg. each to assist maximal absorption.[6] With the continued intensive therapy, the eosinophil count fell progressively, and the operation terminated successfully.

Fig. 7 shows the laboratory data available on this patient. More pertinent to this discussion is the fact that during a period of hypotension on the first postoperative day the patient failed to respond to blood transfusion (there was no blood loss) but promptly responded to intravenous adrenocortical extract; this occurred when serum electrolyte levels would suggest hypoadrenocorticism. The rest of this patient's convalescence was remarkably uneventful, and the method of employing ACTH in withdrawing cortisone is demonstrated in Fig. 7.

CASE 4 (37-74-90).—S. L., a 42-year-old white man, had a diagnosis of carcinoma of the stomach; prior tests showed an intact and responsive pituitary-adrenocortical system. A radical total gastrectomy and total pancreatectomy were performed without event. A

Fig. 5.



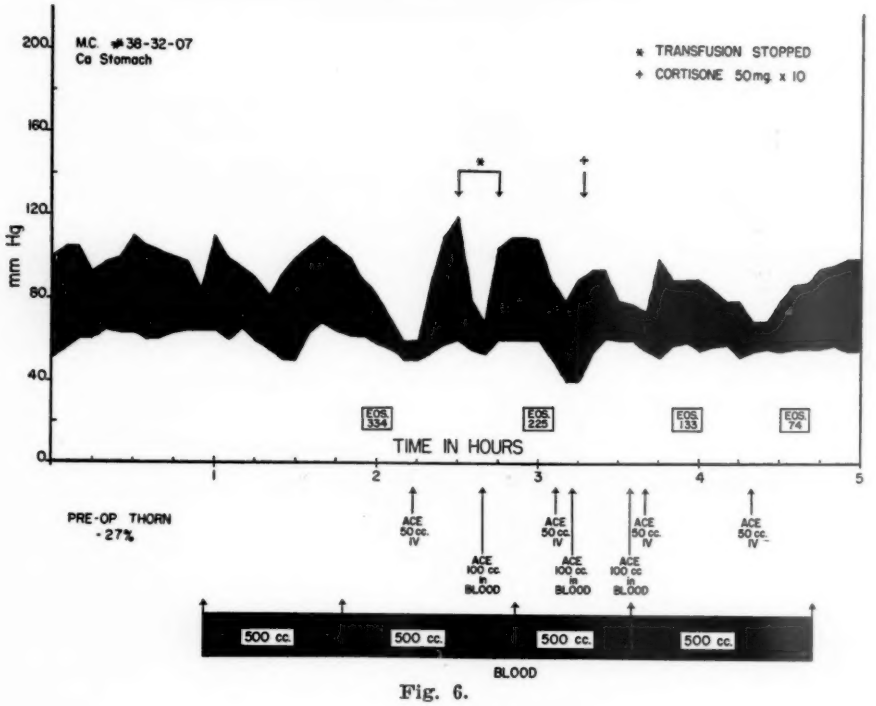


Fig. 6.

Fig. 5.—Pertinent data from the anesthesia record of Case 2. (See text for details.)

Fig. 6.—Pertinent data from the anesthesia record of Case 3. *EOS* represents number of eosinophils per cubic millimeter of blood. *TRANSFUSION STOPPED,* Because of mechanical difficulties, the blood infusion temporarily was interrupted over this period. (See text for details.)

moderately severe degree of hypotension, which did not respond to repeated blood transfusions, appeared on the second postoperative day. It has been demonstrated that an adequate available supply of adrenocortical steroids will prevent ketonemia or ketonuria in a severely diabetic individual.[9, 12] For this reason it is interesting to correlate three evidences of adenocortical insufficiency in this patient: hypotension, high eosinophil count, and ketonuria (Fig. 8). Aqueous adrenocortical extract was given by slow intravenous infusion for a three-day period. It is quite significant that the hypotension was corrected simultaneously with the fall in eosinophils and disappearance of ketonuria, although there had been no change in the fasting blood sugar level and the insulin dosage was essentially constant, but at a low level. The only conclusion to be made from these observations is that the hypotensive state was one manifestation of relative hypoadrenocorticism.

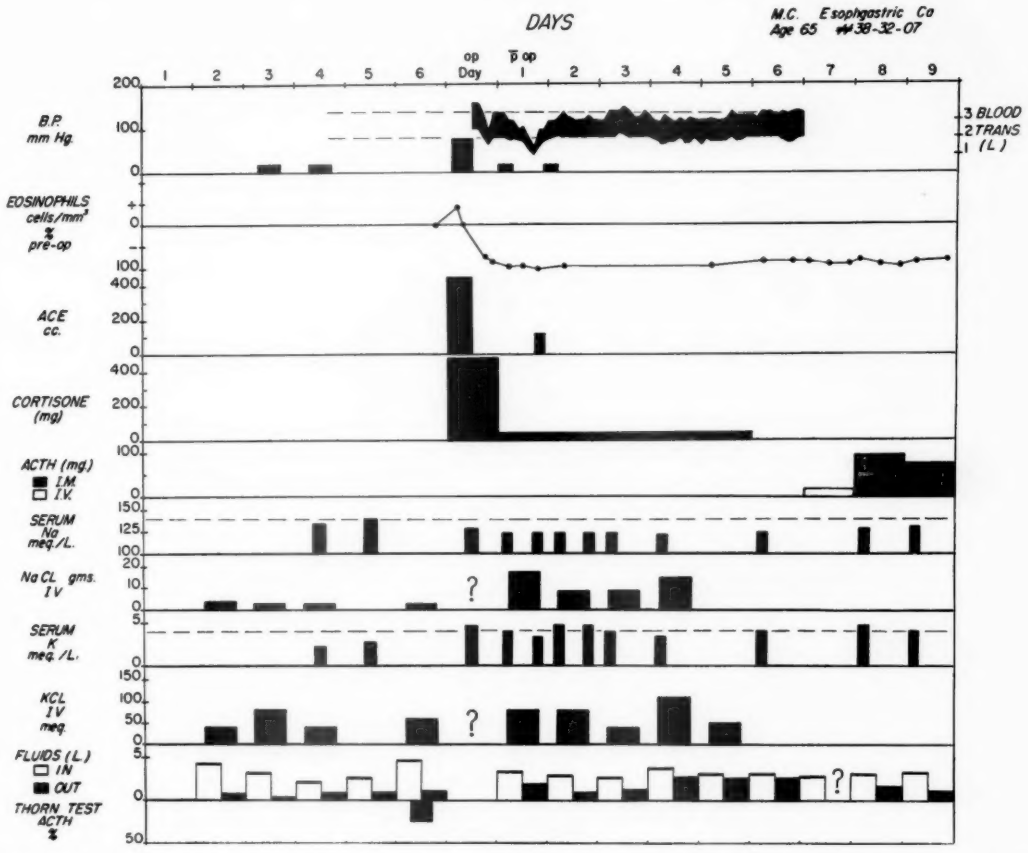


Fig. 7.—Essential clinical data from the record of Case 3, including the preoperative Thorn test. (See text for details.)

CASE 5 (C31696).—F. P., a 63-year-old white man, was first admitted to the hospital twenty-four hours after the perforation of a gastric ulcer, in severe shock and with generalized peritonitis. The left portion of Fig. 9 illustrates pertinent data obtained during the first hospitalization period. Vertical time relationships are portrayed accurately. It is readily apparent that the severe clinical shock did not respond to the administration of 1,500 c.c. of whole blood. An eosinophil count was moderately elevated at a time when it presumably should have been very low. The administration of 150 c.c. of aqueous adrenocortical extract was followed by a prompt rise in blood pressure, clinical improvement, and a fall in eosinophil count. The hemodynamic state began to deteriorate again, and another transfusion was given with no change in the progressing fall in blood pressure

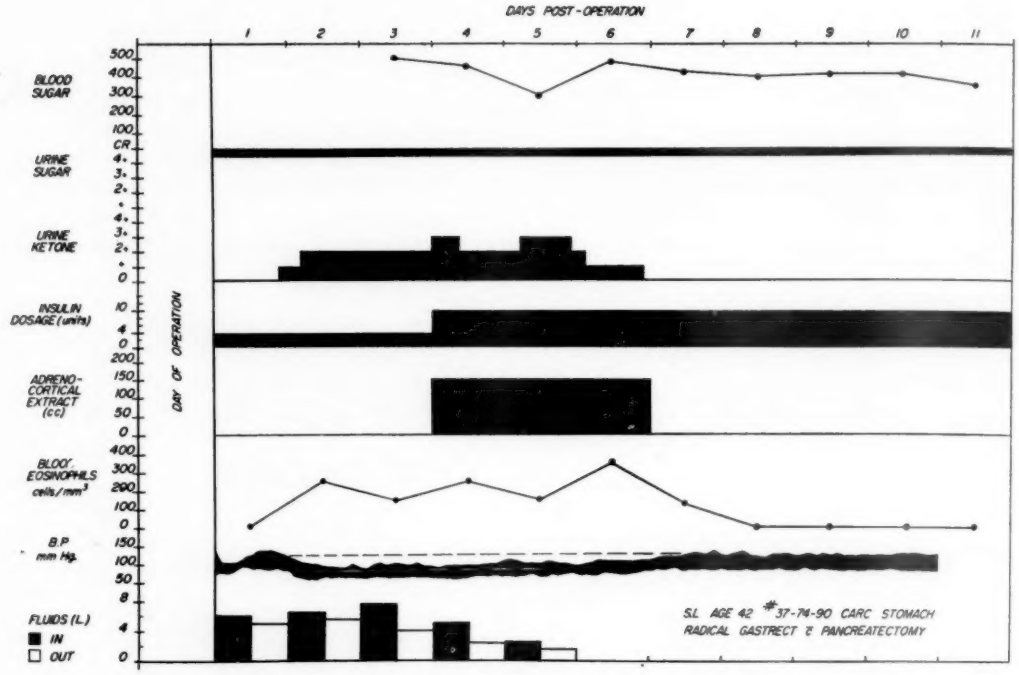


Fig. 8.—Clinical data from Case 4. Note the simultaneous disappearance of three evidences of adrenocortical insufficiency: hypotension, high eosinophil count, and ketonuria. (See text for details.)

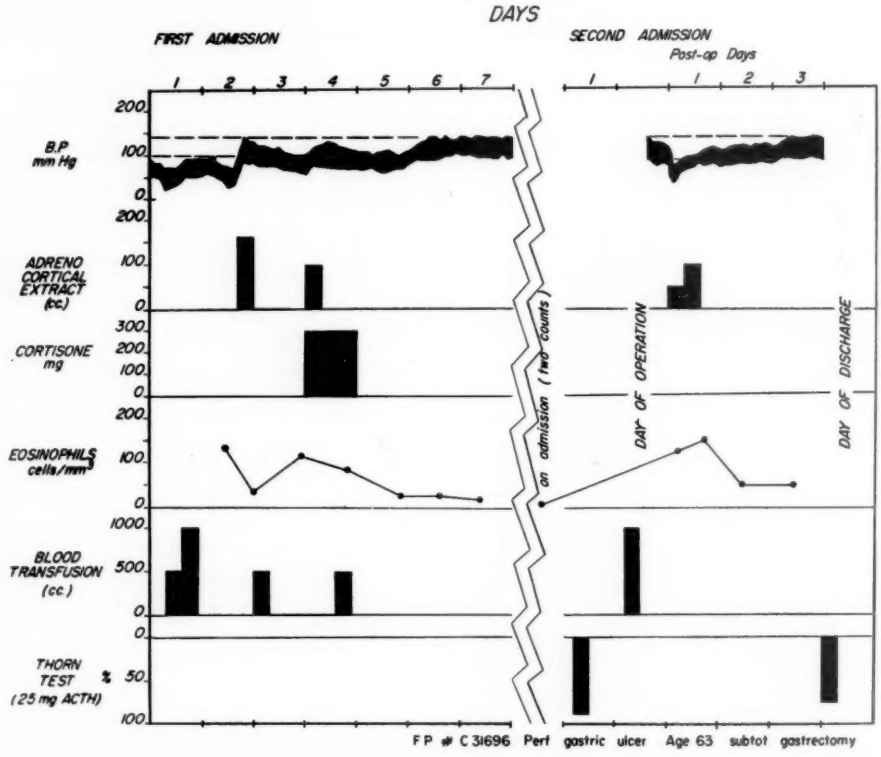


Fig. 9.—Data from the two hospital admissions of Case 5. Note shock, which does not respond to blood transfusions but does respond to adrenocortical extract, occurring during both admissions despite two low normal Thorn tests during the second. (See text for details.)

and rise in eosinophil count. Aqueous adrenocortical extract, 100 c.c., was given with an appropriate rise in blood pressure. Simultaneously, 300 mg. of cortisone acetate was given intramuscularly. Another 500 c.c. of whole blood did not alter the hypotensive state. Approximately thirty-six hours after the cortisone had been given, the eosinophil count had fallen to a satisfactory level, and at that time the blood pressure stabilized. Twenty-four to thirty-six hours is the generally accepted time interval required for a single intramuscular injection of cortisone to produce its maximal therapeutic effect. The subsequent convalescence was uneventful under nonoperative management, and the patient was discharged with a return date six weeks later for a gastric resection.

Forewarned of possible adrenocortical hypofunction, an ACTH-eosinophil (Thorn) test was performed on admission with a 95 per cent fall, a very satisfactory test, as shown in the right half of Fig. 9. The operative procedure was carried on without event. In the immediate postoperative period, shock, which was in no way deterred by 1,000 c.c. of whole blood, supervened, and a high eosinophil count was found. Aqueous adrenocortical extract significantly improved the hypotension and caused a fall in eosinophils. The remainder of the postoperative convalescence was without incident. An ACTH-eosinophil test made the day of discharge again demonstrated a normally responding adrenal cortex by that test.

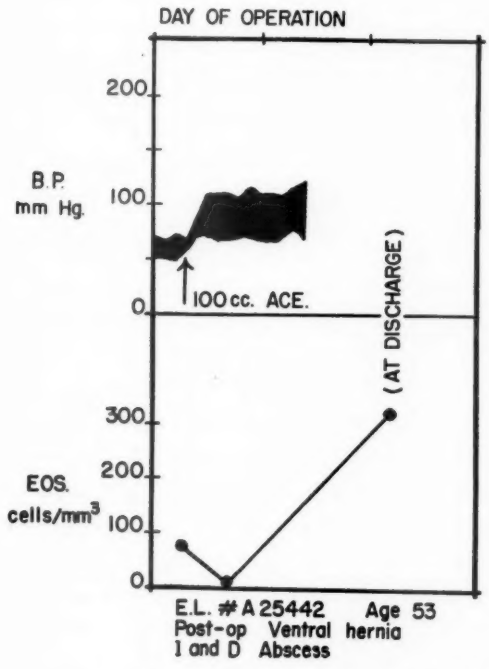


Fig. 10 (Case 6).—(See text for details.)

Case 6 (A25442).—E. L., a 53-year-old white man, had had a ventral hernia repaired two months prior to the present admission. The current hospitalization was for an incision and drainage of a large wound abscess. No evaluation of pituitary-adrenocortical function was made. In the immediate postoperative period, a state of moderately severe shock occurred. Realizing that this state might have been easily corrected by pressor agents or blood transfusion, we decided to administer a therapeutic trial of adrenocortical extract. The eosinophil count during the shock state was higher than that usually seen in the normal postoperative period. Fig. 10 demonstrates the dramatic blood pressure response to the extract occurring simultaneously with a fall in the eosinophil count.

CASE 7 (38-57-50).—E. S. was a 30-year-old white woman, gravida ii, para i. She was four months pregnant and was admitted because of vaginal bleeding and fever, having passed per vaginam a small bone about twelve hours previously. The final diagnosis was: Rh_0 mother with a dead fetus. A manual extraction of the macerated fetus was performed, and the subsequent severe bleeding required packing. The patient bled through the packs, and a total hysterectomy was performed for a ruptured uterus. At the time of laparotomy it was discovered that the pregnancy had been a cervical implantation, with rupture of the cervix and laceration into the uterine artery on the left. Estimated operative blood loss was 6,000 c.c.; replacement was 7,000 c.c. During operation, the generalized bleeding syndrome characteristic of an incompatible blood transfusion was noted, and whole fresh blood was begun. The hemorrhagic diathesis apparently was brought under control, but the patient's blood pressure remained at 80 mm. Hg systolic and 40 mm. Hg diastolic, irreversible to further transfusion. At this time the patient had received 8,000 c.c. of whole blood. The eosinophil count at this time was 89 cells per cubic millimeter, much higher than had been anticipated. A test dose of 50 c.c. of aqueous adrenocortical extract was given, and the blood pressure immediately but transiently rose to 110 mm. Hg systolic. An immediate infusion was started consisting of 200 c.c. of aqueous adrenocortical extract in 500 c.c. of 5 per cent dextrose in distilled water. The blood pressure rose and stayed within a normal range. A hematocrit taken at this time was 26 per cent. The patient then received two 500 c.c. blood transfusions, each containing 200 c.c. of aqueous adrenocortical extract. The blood pressure stabilized completely at 110 mm. Hg during and following the transfusions, and eosinophil counts were stationary, showing 0 cells per cubic millimeter. No shock state recurred during the remainder of the convalescence.

DISCUSSION

When individuals are subjected to a stress, a rise instead of the anticipated fall in the numbers of eosinophils and lymphocytes can be produced experimentally by maintaining them on a fixed available level of adrenocortical steroids; furthermore, the magnitude of these increases qualitatively parallels the severity of the stress.[10] A clinical counterpart of this phenomenon has been demonstrated amply in the patterns of response in the first part of this study. When the rate of peripheral-tissue utilization of adrenocortical steroids exceeds their availability, the eosinophil count rises. In general, it would appear that the rate of adrenocortical hormone utilization parallels cellular activity and that the hormone is necessary for the mobilization of energy for cellular work. It is quite reasonable that the increased cellular activity which accompanies homeostatic adjustments to stress may be responsible at least in part for the parellel increase in the rate of utilization of adrenocortical hormone[17] and its increased production. At any time of stress during which an elevated eosinophil count can be demonstrated, this fact can be taken as direct evidence for an insufficient supply of adrenocortical hormone.

With the more complete understanding of the pathophysiology of "irreversible" shock and the demonstration that some of the criteria for irreversibility can be improved by the administration of adrenocortical steroids, an avenue for a better evaluation of clinical shock can be found. If a patient is in shock, irreversible to adequate blood replacement, and the eosinophil count is not at the anticipated low level, it is reasonable to assume that an adequate supply of adrenocortical hormone is not available because of hemodynamic failure. In this state, a condition of temporary peripheral adrenocortical in-

sufficiency is present, and a beneficial response in the shock state could well be obtained by therapy with an adrenocortical preparation suitable for rapid intravenous administration. Since there are tremendous demands for adrenocortical hormone in stress, large amounts are necessary for adequate treatment. It may be necessary in some cases to give a test dose of adrenocortical extract (50 c.c.) and to follow the blood pressure; if relative adrenocortical failure is fundamental to the problem, a dramatic and instantaneous, yet transient, response in blood pressure and pulse quality obtains.

It is quite true that several of the patients discussed in this report were endocrinologically abnormal, but the important fact remains that, by ordinary careful histories, physical examinations, and routine laboratory tests, no evidences of endocrinopathic stigmata were revealed. Other patients in this series were endocrinologically normal, at least as far as the tests employed were concerned, yet the stress to which they were subjected exceeded the ability of the adrenal cortex to contend with it. Shock, irreversible by established clinical criteria, supervened.

SUMMARY

Various patterns of adrenocortical response to the trauma of surgical procedures have been presented. The configuration of the pattern depends on the severity of the incurred stress and the availability of endogenous adrenocortical hormone to effect the necessary homeostatic readjustments.

The adrenal cortex incontrovertibly can be implicated in the pathophysiology of irreversible shock when blood replacement is followed by no beneficial response and the level of circulating eosinophils is above a very low level.

The more careful evaluation of the integrity of the pituitary adrenocortical mechanism prior to operation is now required.

In some cases, because of hemodynamic failure in the shock syndrome, a temporary period of relative hypoadrenocorticism may supervene. This complication may be an important contributor to the perpetuation of the shock state with an irreversible outcome.

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SOME PHYSICAL-CHEMICAL PROPERTIES OF POLYVINYLPYRROLIDONE

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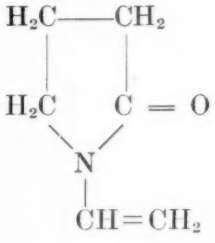
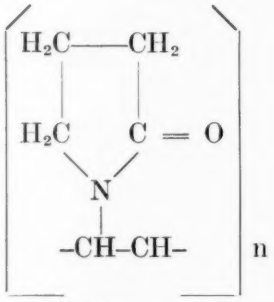
POLYVINYLPYRROLIDONE (PVP) is a water-soluble, high molecular weight polymer with chemical and physical properties desirable in a plasma extender. It is prepared from acetylene by processes devised by Reppe[2] in 1938. The last stage in the process, polymerization of the monomer, N vinyl pyrrolidone, is carried out in aqueous solution with hydrogen peroxide as catalyst, the concentration of the latter controlling the degree of polymerization.



Monomer



Polymer

Commercial preparations, suitable for use as plasma expanders, are mixtures of the polymer chains, averaging 35,000 to 40,000 molecular weight, with no residual monomer. The latter is appreciably toxic, but is readily identified by virtue of its unsaturation, and is easily extracted with methylene chloride.

The polymer is an undissociated, neutral substance. There is some evidence that the chains of from 150 to 720 units end in acid radicals, which would account for a minimal electrophoretic mobility. The hydrophilic properties are probably assignable to the $\diagdown$N—C=O$\diagup$ groups.

Following Starling's dictum that only "colloidal" hydrophilic substances could be efficacious in replacement therapy, Hecht and Weese[1] first evaluated PVP as a plasma expander. Their initial criteria were that the material had to be hydrophilic and chemically indifferent, and a solution of the material should approximate that of the plasma proteins in molecular weight and viscosity.

This study was supported by a grant from Schenley Laboratories, Inc., 350 Fifth Avenue, New York.

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Some of the chemical and physical properties of PVP-Macrose* relative to these criteria are included in this report. Clinical experience will appear in other articles.[5]

TITRATION DATA

PVP-Macrose has no groups titrable by either acid or alkali. The pH titration curve (Fig. 1) was determined electrometrically by titration according to standard procedure. PVP exhibits no appreciable buffer capacity, and therefore cannot contribute to, or directly disturb, the acid-base of the recipient. Any electrolyte alterations following PVP administration, if they occur, must then be referable to the saline vehicle employed, or to the physiologic response of the recipient. Numerous serum sodium, potassium, and chloride estimations, before and after PVP, showed that changes in serum electrolytes were within normal limits.

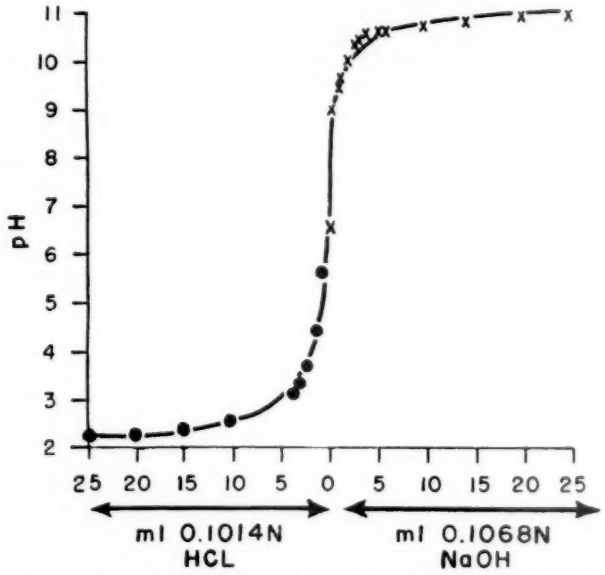

Fig. 1.—Titration curve of PVP-Macrose with standard HCl and NaOH.

ULTRACENTRIFUGAL DATA

The molecular size and size distribution have been determined by industrial procedure in which high polymers are commonly characterized by the K-value, which is a function of viscosity. Solutions with K-values between 28 and 32 are suitable for clinical use. The average molecular weights corresponding to these figures are 30,000 to 40,000 units, no more than 10 per cent of the 15,000-molecular-weight polymer. The distribution had been confirmed by fractionation of the material.

A 3.5 per cent solution of PVP-Macrose in 0.9 per cent NaCl was subjected to centrifugation in the analytic ultracentrifuge.† The pattern obtained (Fig. 2) illustrates the gaussian distribution of the components. The

*PVP-Macrose supplied by Schenley Laboratories, Inc., New York.
†Specialized Instrument Co., Model E.

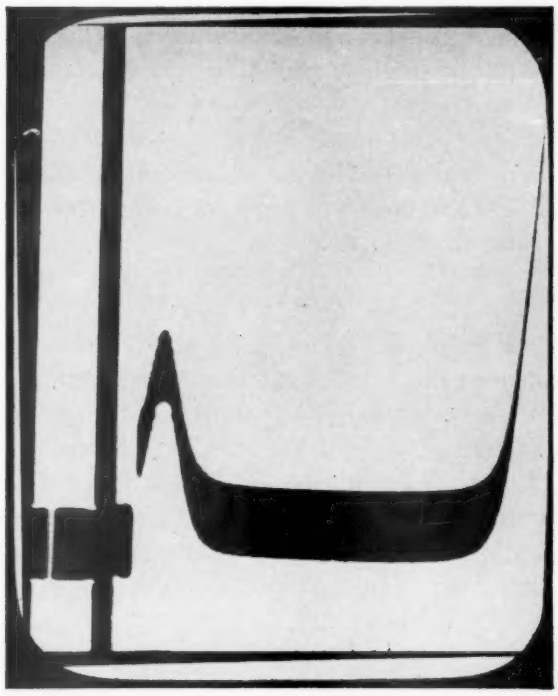

Fig. 2.—Ultracentrifugal pattern of PVP in 0.9 per cent NaCl after forty minutes at 60,000 r.p.m.

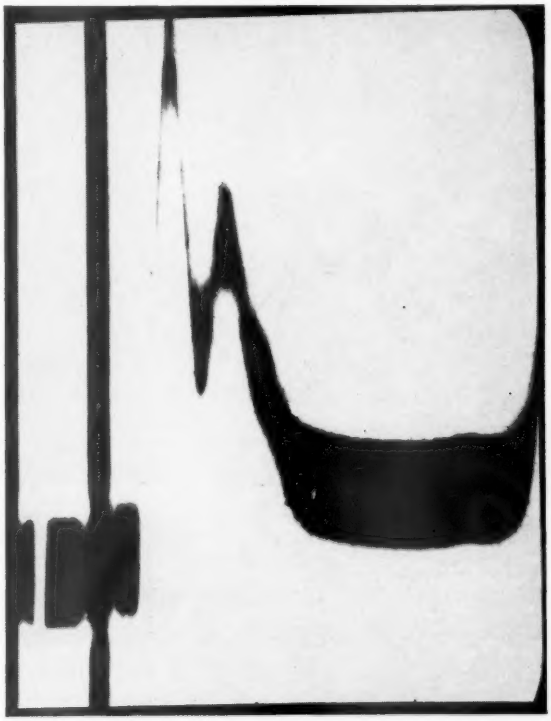

Fig. 3.—Ultracentrifugal pattern of PVP and serum after sixty minutes at 60,000 r.p.m.

average molecular weight, calculated from the sedimentation constant (S_{20} w = 0.9 S) and an assumed diffusion constant of 4×10^{-7} cm. per second, is about 40,000. These data are consistent with those obtained by viscosity and light-scattering techniques.

The ultracentrifugal pattern of PVP-Macrose mixture indicates a sharp separation of the apparently undiluted components (Fig. 3). It may be of some significance that PVP does not appear to combine with serum proteins or otherwise affect their distribution.

ELECTROPHORETIC DATA

As expected, PVP exhibits low mobility at pH 8.6 in the Tiselius apparatus.* The serum protein migrated with the characteristic mobilities without apparent interaction between the PVP and the serum proteins. The PVP migrated with the gamma globulin fraction of the serum in all cases examined (Fig. 4). Electrophoretic examination of the serum following PVP administration was carried out at intervals in several cases. The data also indicated that PVP was present in the serum in appreciable amounts up to twenty-four hours after administration. In general, however, PVP can no longer be detected after one week (Table I).

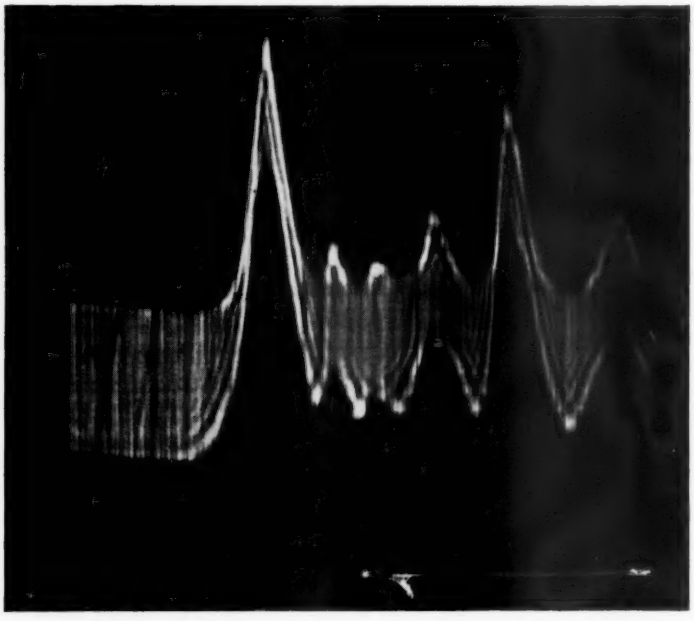

Fig. 4.—Descending electrophoretic pattern of PVP and blood serum in 0.1 ionic strength, diethylbarbiturate buffer of pH 8.6 after sixty minutes at 10.6 volts per centimeter.

ESTIMATION OF PVP IN SERUM AND URINE

PVP in low concentration reacts with I_2 to produce a colored compound absorbing maximally at 5,000 Å and obeying the Beer and Lambert laws. $Zn(OH)_2$ filtrates were employed for serum analysis.

*Perkin-Elmer Corp.

The amount of PVP excreted in the urine was determined by adapting the method of Thrower and Campbell.[4] PVP forms with iodine a colored complex which absorbs maximally at 5,000 Å and follows Beer's law of concentration dependence from 0 to 35 μg per milliliter of PVP. For most samples, urine was diluted 1:1,000 with 0.2 molar citric acid, an aliquot of 10 ml. was withdrawn, and 2 ml. of KI_3 reagent (13.5 Gm. of sublimed iodine dissolved in an aqueous solution containing 24 Gm. of KI and diluted to approximately

TABLE I. SERUM PVP ASSAY BY ELECTROPHORETIC METHODS

PATIENT AND WEIGHT (KG.)	AMOUNT GIVEN	TIME	TOTAL PROTEIN (GRAMS PER 100 C.C.)	COMMENT ON ELECTROPHORETIC PATTERN
C.,	500 c.c.,	Control	7.17	*
55.6	17.5 Gm.	8 days	7.08	*
		17 days	7.06	
R.,	500 c.c.,	Control	6.68	*
63.9	17.5 Gm.	8 days	6.49	
B.,	500 c.c.,	Control	6.86	
80.4	17.5 Gm.	8 days	6.82	*
W.,	500 c.c.,	Control	7.38	
70.6	17.5 Gm.	8 days	6.74	*
H.,	500 c.c.,	Control	6.94	*
78.1	17.5 Gm.	14 days	6.90	
F.,	1,000 c.c.,	Control	6.49	*
57.6	35 Gm.	8 days	6.52	*
	1,000 c.c.,	Control	6.70	
	35 Gm.	24 hr.	5.13	Little PVP detectable
Wh.,	500 c.c.,	Control	7.40	*
54.9	17.5 Gm.	8 days	7.64	*
Re.,	1,000 c.c.,	Control	6.60	
62.5	35 Gm.	24 hr.	5.26	Definite PVP peak
M.,	1,000 c.c.,	Control	5.41	
58.0	35 Gm.	6 days	5.50	Presence of PVP questionable
S.,	1,000 c.c.,	Control	6.20	
64.1	35 Gm.	24 hr.	5.98	*
J.,	1,000 c.c.,	No control		
58.3	35 Gm.	12 hr.	6.57	Presence of PVP questionable
Lu.,	1,000 c.c.,	Control	6.20	
44.6	35 Gm.	24 hr.	5.43	Presence of PVP questionable
Sm.,	2,000 c.c.,	Control	8.15	
70.5	70 Gm.	6 hr.	6.12	Definite PVP
		24 hr.	6.18	Definite PVP
		16 days	6.35	Little PVP
Wi.,	2,500 c.c.,	Control	6.92	
15.6	87.5 Gm.	6 hr.	4.56	Definite PVP
		24 hr.	4.20	Definite PVP
Br.,	3,000 c.c.,	Control	7.07	
83.4	105 Gm.	12 hr.	4.43	Definite PVP
		36 hr.	4.37	Definite PVP
He.,	1,000 c.c.,	Control	5.82	
62.5	35 Gm.	24 hr.	4.96	Definite PVP

*No observable peak or elevation due to presence of PVP.

0.0006 normal) was added. The solution was swirled, a portion was transferred to a 1 cm. cuvette, and the absorption read at 5,000 Å on a Beckman DU spectrophotometer. The readings were compared with those obtained with known concentrations of PVP which were plotted on graph paper.

At this low concentration there is no interference from anything in urine. In serum, however, it is necessary to remove the proteins which would other-

wise react with some of the iodine. This was done by the Somogyi zinc hydroxide precipitation.[3] After the proteins had been precipitated, the filtrate was treated in the same way as urine, except that it was only necessary to make a 1:500 dilution to bring it within the correct concentration range.

TABLE II. PVP EXCRETION IN URINE AND DETERMINATION OF PVP IN SERUM: TWENTY-FOUR HOURS POSTINFUSION

PATIENT	AMOUNT OF PVP ADMINISTERED (GM.)	AMOUNT OF PVP EXCRETED IN 24 HOURS (GM.)	AMOUNT OF PVP RETAINED (GM.)	TOTAL PLASMA VOLUME POST-PVP (C.C.)	THEORETICAL CONCENTRATION OF PVP IN SERUM (MG. PER C.C.), RETAINED PLASMA VOLUME (GM.)	OBSERVED CONCENTRATION OF PVP IN SERUM (MG. PER C.C.)
B. F.	35	19.1	15.9	2,325	6.8	4.7
F. L.	35	7.4	27.6	3,435	8.0	3.4
T. W.	35	22.9	12.1	3,226	3.7	3.4
D. R.	35	6.8	28.2	2,948	9.6	4.6
J. F.	35	16.6	18.4	2,516	7.3	3.9
H. L.	35	19.6	15.4	2,490	6.2	4.2
M. H.	35	9.9	25.1	3,319	7.6	3.4
A. B.	35	17.1	17.9	2,802	6.4	4.2

SUMMARY

Polyvinylpyrrolidone is a chemically inert, hydrophilic, water-soluble macromolecule, averaging 35,000 to 40,000 molecular weight. Solutions of PVP have minimal buffer capacity, and electrophoretic and ultracentrifugal analyses indicate no interaction between it and plasma proteins.

Chemical and electrophoretic methods of qualitative and quantitative estimation of PVP in serum and urine have been reviewed.

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HYPERCHLOREMIC ACIDOSIS FOLLOWING ANTERIOR PARTIAL AND COMPLETE PELVIC EXENTERATION

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WITH the increasing frequency of ureterointestinal anastomoses and the formation of wet colostomy in the extended treatment of cancer in the pelvis, attention is drawn to the possibilities of physiologic imbalances resulting from such alterations in the urinary tract. When urine is excreted into the lower colon, a situation foreign to the normal status obtains in that urine, instead of pooling temporarily in the bladder and then being excreted, is pooled in the lower colon and then excreted. The colon itself possesses certain absorptive potencies for substances excreted by the kidneys. The absorption of these substances into the blood stream to be again excreted by the kidney and again poured into the colon conceivably may and does result in certain deviations from normal in regard to chloride levels, acid-base balance, and urea concentration of the circulating plasma.

Clinical experience (A. B.) has shown that, in the large majority of patients subjected to these operations, the subsequent course is clinically asymptomatic in so far as the acid-base balance is concerned, that imbalances detectable by laboratory studies may be present but seem to be asymptomatic, or that a clinical syndrome does supervene in the presence of the imbalance (one patient). Clinically the disturbance, if it occurs, is said to be characterized by (a) fatigability, (b) constant asthenia of varying degree, (c) anorexia, (d) a perverted sense of taste, (e) nausea, sometimes vomiting, (f) loss of weight, and (g) a general feeling of not being well without special emphasis on particular symptoms. Laboratory studies reveal elevated plasma chlorides, lowered carbon dioxide-combining power, and elevated blood urea nitrogen. The syndrome is referred to as "hyperchloremic acidosis," and has been previously discussed in the recent literature.[1-3] Hyperchloremia and depressed plasma carbon dioxide-combining power may obtain in the presence of essentially normal blood urea nitrogen levels.

This report is concerned with two groups of patients, namely, those who received anterior partial exenteration, removal of bladder, vagina, uterus, and pelvic lymph nodes with implantation of the ureters into the intact colon (Fig. 1), and those who received total pelvic exenteration with implantation of ureters into the sigmoid above the end colostomy, a wet colostomy[4, 5] (Fig. 2).

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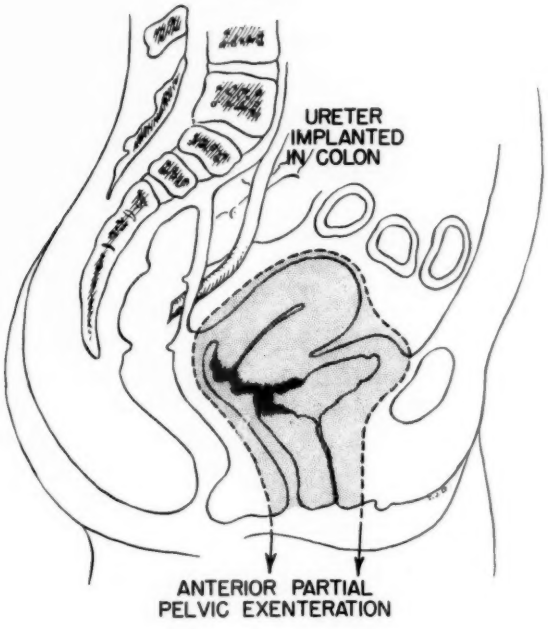
In those patients who received anterior partial pelvic exenteration the anal sphincter mechanism is intact, and the urine excretion is under voluntary control. Under these circumstances there is obviously periodic retention of urine in the colon, especially at night, and there is greater opportunity for

Fig. 1.



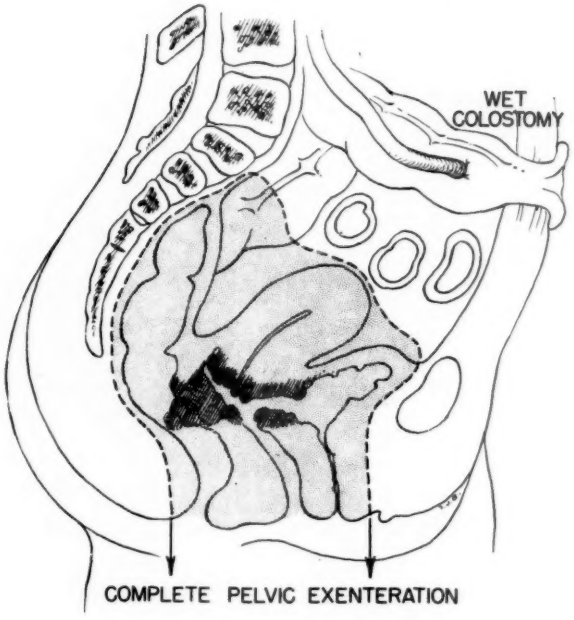


Fig. 2.

Fig. 1.—Diagram of anterior partial pelvic exenteration showing ureters implanted into pelvic colon which is undisturbed.

Fig. 2.—Diagram of total pelvic exenteration showing ureters implanted into sigmoid end colostomy to form a wet colostomy.

absorption of urinary contents into the circulation. As of March 1, 1953, over eighty of these operations had been performed. In Table I a summary is presented of records of seventeen patients selected more or less at random from the survivors ranging from two weeks to five years. It is felt that if significant imbalances are to occur in the absence of other complicating factors, they would develop during these periods. In the patients who died with recurrences or who died during the immediate postoperative period, acid-base imbalance was never observed to be the cause of death.

TABLE I. URETERS IMPLANTED INTO THE COLON (ANTERIOR PELVIC EXENTERATION)

PATIENT	AGE AT OPERATION (YEARS)	PLASMA CHLORIDES (NORMAL: 98-106 MEQ. PER LITER)		CARBON DIOXIDE (23-31 MEQ. PER LITER)	BLOOD UREA NITROGEN (8-15 MG. PER 100 C.C.)	INTRVENOUS PYELOGRAMS
1	53	Preop.	97	23	15.0	
		P.O. 2 wk.	102	22	8.5	
2	54	Preop.	97	22	19.8	
		P.O. 2 wk.	105	18	14.0	
3	34	Preop.	106	20	15.7	
		P.O. 6 mo.	113	23	11.1	
4	51	Preop.	107	27	9.1	
		P.O. 10 mo.	101	19	13.8	Moderate bilateral hydronephrosis
5	48	Preop.	112	25	16.4	
		P.O. 11 mo.	120	18	72.0	Slight hydronephrosis, left; marked impaired kidney function, right
6	58	Preop.	110	–	12.2	
		P.O. 1 yr.	106	20	21.8	No hydronephrosis
7	66	Preop.	97	–	13.0	
		P.O. 1 yr., 1 mo.	99.7	22.3	17.2	Marked bilateral hydronephrosis
8	58	Preop.	108	25	11.2	
		P.O. 1 yr.	122	15	20.1	Slight hydronephrosis
9	43	Preop.	110	–	8.8	
		P.O. 1 yr., 4 mo.	98.6	23	8.3	
10	62	Preop.	106	23	12.0	
		P.O. 1 yr., 10 mo.	113	19	19.8	No hydronephrosis
11	71	Preop.	103	22	15.6	Normal right kidney;
		P.O. 1 yr., 6 mo.	107	24	20.6	poor visualization, left kidney
12	48	Preop.	93	27.3	10.0	
		P.O. 2 yr., 6 mo.	100	–	17.2	Slight bilateral hydronephrosis
13	63	Preop.	–	–	–	
		P.O. 3 yr., 9 mo.	119	17	26.1	
14	65	Preop.	–	–	–	
		P.O. 3 yr., 4 mo.	100	22	16.0	No hydronephrosis
15	47	Preop.	94.3	27	16.5	
		P.O. 3 yr., 10 mo.	109	17	37.0	Slight bilateral hydronephrosis
16	44	Preop.	99.5	–	18.0	
		P.O. 4 yr.	107	33	14.8	Slight hydronephrosis
17	54	Preop.	98	–	10.0	Slight bilateral hydronephrosis; right nephrolithiasis
		P.O. 5 yr.	105	20	12.0	

In the seventeen patients studied, eight presented at least one abnormal finding among the three chemical determinations (Cases 2-4, 6, 7, 11, 12, 16). In five (Cases 5, 8, 10, 13, 15), the classical chemical features of hyperchloremic

acidosis were present, that is, elevated plasma chlorides, depressed carbon dioxide-combining power, and elevated blood urea nitrogen. In four of these the clinical symptoms associated with this syndrome were absent at the time the blood was drawn, and hence no treatment was instituted. Case 15 has moderately severe diabetes which she controls with insulin herself "by the way she feels," since tests upon the urine passed per rectum are not reliable. The excellent clinical status of Case 5 completely belies the blood chemical findings, although she is being carefully observed. On one occasion she complained of a peculiar taste in her mouth, the only symptom ever presented. She was advised to increase her water intake during the day and to take .3 Gm. of sodium bicarbonate four times a day for four days; the symptom disappeared, and the blood urea nitrogen and chlorides returned to nearer normal levels. Case 16 had an attack of food poisoning the day prior to having the blood sample drawn and was taking large doses of sodium bicarbonate by mouth; this probably accounts for the alkalosis observed. Subsequently this has disappeared.

In the wet colostomy the ureters are implanted into the sigmoid colon proximal to the end colostomy. There is no sphincteric mechanism, and the urine is readily discharged more or less at a constant rate or frequently with peristalses. However, in some instances appreciable quantities of urine may pool in the sigmoid and even flow up to the proximal descending or left transverse colon. Under the latter conditions increased opportunity for absorption of urinary products obtains, and there is the possibility of hyperchloremic acidosis.

In Table II are summarized the data in twenty patients selected more or less at random and including some of the three- to five-year survivors with wet colostomy. In five instances (Cases 1, 3, 8, 17, 19) the available data indicated essentially no imbalances. In nine patients (Cases 6, 7, 9, 10, 12-15, 18) one of the factors showed deviation from normal. In none of these was the carbon dioxide-combining power of the plasma altered. In four there was hyperchloremia, and in five there was slight elevation of the blood urea nitrogen. In four patients (Cases 2, 4, 11, 16) there were two abnormal findings in each. One showed hyperchloremia and slight elevation of blood urea nitrogen, while in three there was decrease in carbon dioxide-combining power and slight elevation in blood urea nitrogen. Only two patients showed all the alterations typical of hyperchloremic acidosis (Cases 5 and 20). They are asymptomatic as far as the hyperchloremic acidosis clinical syndrome is concerned, and now survive three and six months to date, respectively, after total pelvic exenteration. The latter patient is working full time as a domestic servant.

DISCUSSION

The plasma chlorides, carbon dioxide-combining power, and blood urea nitrogen in seventeen patients who received anterior pelvic exenteration with implantation of ureters into the intact colon are compared with similar observations made in twenty patients who received total pelvic exenteration with wet colostomy. Among the former there were five instances of the typical

chemical abnormalities associated with hyperchloremic acidosis, as compared to two among those with wet colostomies. There were eight patients with partial exenterations who had one abnormal factor, compared to nine among those with wet colostomies. There were four in the partial exenteration group who showed normal findings, compared with five in the wet colostomy series.

TABLE II. WET COLOSTOMY (TOTAL PELVIC EXENTERATION)

PATIENT	AGE AT OPERATION (YEARS)	PLASMA CHLORIDES (NORMAL: 98-106 MEQ. PER LITER)		CARBON DIOXIDE (23-31 MEQ. PER LITER)	BLOOD UREA NITROGEN (8-15 MG. PER 100 C.C.)	INTRAVENOUS PYELOGRAMS
1	48	Preop.	111			
		P.O. 2 mo.	100	21	11.6	
2	32	P.O. 2 mo.	96	19	17.3	
3	48	P.O. 3 mo.	101	26	-	
4	58	Preop.	104	18	9.2	
		P.O. 5 mo.	101	19	22.4	
5	59	Preop.	109	21	15.5	Moderate bilateral hydronephrosis
		P.O. 6 mo.	110	20	18.8	
6	42	P.O. 11 mo.	110	22	11.8	Slight hydronephrosis
7	47	Preop.	112	21	8.0	Moderate hydronephrosis
		P.O. 1 yr.	108	20	12.6	
8	35	Preop.	104	-	14.4	Marked bilateral hydronephrosis
		P.O. 1 yr.	106	-	15.8	
9	48	Preop.	105	-	7.2	
		P.O. 1 yr., 3 mo.	97	22	19.0	
10	41	Preop.	105	-	7.4	
		P.O. 1 yr., 10 mo.	102	22	23.0	
11	50	Preop.	101	-	11.0	
12	61	P.O. 1 yr., 5 mo.	114	-	22.0	Moderate hydronephrosis, left; no function, right
		Preop.	114	24	12.6	
		P.O. 2 yr., 2 mo.	105	-	23.8	Slight bilateral hydronephrosis
13	39	Preop.	101	-	12.0	
		P.O. 3 yr.	99	26	20.0	No hydronephrosis
14	63	Preop.	103	-	9.6	
		P.O. 3 yr., 4 mo.	109	26	28.0	Bilateral moderate hydronephrosis
15	32	P.O. 4 yr.	112	22	-	
16	47	Preop.	98	-	-	
		P.O. 5 yr.	107	17	26.0	Slight bilateral hydronephrosis
17	31	P.O. 1 day	103	-	28.0	
		P.O. 5 yr., 1 mo.	109	24	18.0	No hydronephrosis
18	57	Preop.	98	-	15.0	
		P.O. 5 yr., 6 mo.	113	22	10.0	Slight bilateral hydronephrosis
19	36	Preop.	103	27.6	8.9	
		P.O. 4 yr., 10 mo.	104	27	12.0	Slight hydronephrosis
20	58	Preop.	107	23	17.8	
		P.O. 3 mo.	115	19	24.5	

Thus, the majority of the patients showed some imbalances, and a total of seven among the whole series of thirty-seven patients showed all the alterations associated with hyperchloremic acidosis (nineteen per cent), while a total of nine of the thirty-seven, that is, 24 per cent, showed no changes. Twelve patients (60 per cent) in the total exenteration group showed slight

elevations of blood urea nitrogen ranging from 17.3 to 28 mg. per cent. Eight patients (43 per cent) among those with partial exenterations showed the blood urea nitrogen to be slightly elevated, ranging from 17.2 to 37, with one patient showing a blood urea nitrogen of 72 mg. per cent. Of special interest in this group of patients, limited in number, is the fact that there was only one instance of clinical symptoms referable to the imbalance, and this was promptly corrected. Thus, in exenteration operations a certain incidence of acid-base and electrolyte imbalance is to be anticipated and accepted. This certainly does not contraindicate the operations. Table III summarizes the comparative incidence of imbalances. There is greater possibility of hyperchloremic acidosis after partial than complete pelvic exenteration. The reason for this is obviously the intact sphincter mechanism after partial exenteration which results in intermittent retention of urine in the lower colon, whereas this is absent in the wet colostomy where urine excretion occurs more or less uninhibited from the colon.

TABLE III. COMPARISON OF IMBALANCES IN PARTIAL AND TOTAL PELVIC EXENTERATION GROUPS

	PARTIAL EXENTERATION (SEVENTEEN PATIENTS)	TOTAL EXENTERATION (TWENTY PATIENTS)
Normal blood chemical findings	4	5
One abnormal determination	8	9
Two abnormal determinations	0	4
"Typical" hyperchloremic acidosis:		
Elevated blood chlorides		
Decreased carbon dioxide-combining power		
Elevated blood urea nitrogen	5 (30 per cent of series)	2 (10 per cent of series)

The mechanisms from the production of hyperchloremic acidosis are not clearly understood. According to Mitchell and Valk[2] it is simply a matter of balance between chloride and fluid intake and urinary passage out of the colon, and that when these factors are in proper relationship absorption of chlorine from the colon is such that hyperchloremia does not occur. On the other hand, Lapides'[3] observations are interpreted by him to indicate that renal tubular damage is the prime etiological factor and that intestinal absorption of urinary contituents is of secondary importance. Experimental studies consisting of urine enemas in three patients with poor renal function and, as controls, urine enemas in three patients with normal renal functions showed that electrolyte imbalance occurred in the former and not in the latter. In one patient operated upon by one of us (A. B.) the preoperative blood urea nitrogen was 74.6 mg. per cent (the plasma carbon dioxide-combining power was 19 meq. per liter and chlorides were 106 meq. per liter) because of obstruction. During the period following total pelvic exenteration, the blood urea nitrogen gradually fell to 35 to 40 mg. per cent after a period of one month, the chlorides were 111 meq. per liter with plasma carbon dioxide-combining power at 16 meq. per liter. Thus, a picture of hyperchloremic acidosis evolved following presumable renal damage due to ureteral obstruction for a period

before operation. This observation supports Lapides' hypothesis. The patient is not included in the series mentioned previously because of the pre-existing renal obstruction.

In years past, various techniques for the creation of artificial bladders have been described and the operations successfully performed in man. Makkas employed the cecum and ascending colon as a bladder, implanted the ureters into the cecum, and employed the appendix as a "urethra." In 1937 Seiffert detached a segment of jejunum, implanted the ureters into one end, and brought the other open end through the abdominal wall. In recent years, interest in these procedures has again developed, and modifications of them have been devised in connection with total pelvic exenteration. Such attempts are praiseworthy and must be carried out in order to learn what might be the preferred method for dealing with the urinary tract following pelvic exenteration. However, in the experience of one of us (A. B.) the wet colostomy has proved satisfactory under the conditions imposed by the radical pelvic en masse visceral excision; five-year survivals have been achieved, and the patients are in full physical activity and quite well adjusted to the wet colostomy. When sufficient long-range survivals from other methods of dealing with the urinary tract after pelvic exenteration are available for comparison, a more definite orientation in this problem will be possible, based on actual experience and presentation of results.

CONCLUSION

While in the series reported by us there was no serious clinical problem posed by the presence of acid-base and electrolyte imbalance, the latter, as shown, was present in varying degree in the majority of instances. Other methods for dealing with the urinary tract in which chemical imbalances might be avoided altogether and which might afford long survival will be worthy, indeed, of consideration.

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THE RELATION OF THE IN VITRO SENSITIVITY TEST TO THE CLINICAL RESPONSE TO AUREOMYCIN THERAPY

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DATA are herewith presented showing that the clinical response to therapy with Aureomycin correlates closely to the results of a properly standardized in vitro sensitivity test to be described in this article.

The test (a modified Rammelkamp-Maxon[1] method).—Aureomycin Hydrochloride, 500 mg., buffered with sodium glycinate is dissolved in 10 c.c. of phosphate-buffered regular broth, pH 7.0. This stock solution is kept at –4° C. Its antibacterial potency does not deteriorate for at least ninety-six hours; it is discarded after this interval.

Immediately prior to making the test, twofold dilutions of the stock solution with phosphate-buffered nutrient broth (Difco), pH 7.0, are prepared, running left to right, from 200 to 0.0125 μg per milliliter. To 1 ml. of each dilution is added 0.1 ml. of an eighteen to twenty-four hour culture diluted so as to contain 500 to 5,000 bacteria per 0.1 ml. A control tube containing 1 c.c. of the buffered broth, to which 0.1 ml. of the diluted culture has been added, is also prepared.

All tubes are then incubated at 37° C. and examined for cloudiness after twenty-four hours.* Reading from left to right, the last macroscopically clear tube is noted. The tubes are incubated for twenty-four hours longer and are again examined. At this time (forty-eight hours) the concentration of the drug in the last macroscopically clear tube is considered to be the minimum bactericidal concentration, because there is no growth on subculture of a large loopful from this tube. The last clear tube after twenty-four hours' incubation, and usually one to three tubes to the left of it, will have become cloudy after forty-eight hours. Although the last clear tube after twenty-four hours does not contain the bactericidal concentration, for purposes of rapid clinical evaluation it may be taken as the measure of the antibacterial effect of the drug on the organism being tested.

The test for each strain was always made twice, the second time two or more days after the first. The results were identical in over 96 per cent of the tests.

From clinical experience with the response to therapeutic doses of Aureomycin (Tables V and VI), strains which are completely inhibited for twenty-

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*Because of the slow growth of hemolytic streptococci and pneumococci the control tube may not become cloudy until more than twenty-four hours have elapsed. The test for these organisms is, therefore, first read six hours after the control tube becomes cloudy and again twenty-four hours later.

four hours by concentrations of 50 μg per milliliter or higher can be classified as resistant; strains inhibited by concentrations of 12.5 to 25 μg per milliliter as borderline, and strains inhibited by concentrations of 6.2 μg per milliliter or lower as sensitive. However, as the following studies show, this classification will not apply if the technique described is not followed in every detail, that is, if use is made of a medium of different composition or of a different pH, or if the reading is done at different time intervals.

Factors Influencing the in Vitro Test.—

Period of incubation: Macroscopically visible growth in tubes containing low drug concentrations appears from two to six hours after growth is noted in the control tube. After twenty-four hours, the last clear tube is usually followed by one to three tubes showing less cloudiness than the control tube, but after forty-eight hours these tubes are just as cloudy as the control. As a rule, one or more of the tubes which are clear after twenty-four hours will also have become cloudy at this time. The last clear tube after twenty-four hours remained the same after forty-eight hours in only 6 per cent of 350 strains tested. There are no further changes of significance on incubation beyond forty-eight hours. This, to some extent at least, may be due to the inactivation of Aureomycin in solution at 37° C.

Influence of the size of inoculum: Using sterile nutrient broth (Difco), a series of tenfold dilutions of a twenty-four hour broth culture of the strain to be tested, ranging from 10^1 to 10^7, were prepared. To each tube was added 0.1 ml. of each dilution in seven duplicate sets of tubes each containing the twofold series of dilutions of Aureomycin described previously.

TABLE I. INFLUENCE OF SIZE OF INOCULUM ON RESULT OF TEST

SAMPLE STRAINS	NUMBER OF BACTERIA INOCULATED	CONCENTRATION OF AUREOMYCIN IN THE LAST CLEAR TUBE (MICROGRAMS PER MILLILITER)	
		AFTER TWENTY-FOUR HOURS	AFTER FORTY-EIGHT HOURS
Escherichia coli (sensitive strain)	2×10^1	0.2	1.6
	2×10^2	0.2	1.6
	2×10^3	0.2	1.6
	2×10^4	0.2	1.6
	2×10^5	0.2	1.6
	2×10^6	0.2	1.6
	2×10^7	0.2	1.6
Nonhemolytic *Staphylococcus albus* (refractory strain)	5×10^1	25	200
	5×10^2	25	200
	5×10^3	25	200
	5×10^4	25	200
	5×10^5	25	200
	5×10^6	25	200
	5×10^7	25	200

The twenty-four and forty-eight hour cultures (Table I) showed identical bactericidal and bacteriostatic titers for twenty of twenty-five strains tested, regardless of the size of the inoculum. In five strains (Pseudomonas 2, hemolytic *Staphylococcus aureus* 2, *Bacillus proteus* 1), the last clear tube

after twenty-four hours' incubation shifted one tube to the left when the inoculum was in excess of 100,000 bacteria, but in four of these strains the results after forty-eight hours were identical regardless of the size of inoculum. In the fifth (*Bacillus proteus*), this shift of one tube to the left persisted after forty-eight hours.

Comment: With this method, the size of the inoculum, as a rule, does not matter. This finding differs from other reported results.[2-4]

Influence of total dose of Aureomycin (varying volume with the same concentration): Five series of tubes containing the usual twofold dilutions of Aureomycin were set up. The volume of fluid in the five tubes of each concentration was 1, 2, 4, 6, and 10 c.c., respectively.

The last clear tube after twenty-four hours and after forty-eight hours had the same concentration in each series for twenty-one of the twenty-five strains tested (Table II). In the remaining four strains (Proteus 1, Pseudomonas 1, *Escherichia coli* 1, hemolytic *Staphylococcus aureus* 1), the tubes containing 6 and 10 ml. at the various concentrations showed, after twenty-four hours, one more clear tube than those containing 1, 2, and 4 ml. But after forty-eight hours all series read exactly alike. Increasing the size of the inoculum did not change the results.

TABLE II. INFLUENCE OF VARYING VOLUMES OF FLUID WITH EQUAL CONCENTRATIONS OF AUREOMYCIN

	VOLUME OF FLUID (MILLILITERS)	CONCENTRATION OF AUREOMYCIN IN THE LAST CLEAR TUBE (MICROGRAMS PER MILLILITER)	
		AFTER TWENTY-FOUR HOURS	AFTER FORTY-EIGHT HOURS
Example characteristic of 21 strains	1	0.05	0.4
	2	0.05	0.4
	4	0.05	0.4
	6	0.05	0.4
	10	0.05	0.4
Example characteristic of 4 strains	1	12.5	25
	2	12.5	25
	4	12.5	25
	6	6.25	25
	10	6.25	25

Comment: It is evident that the concentration of the drug, not the total amount, is the determining factor.

Influencing of pH: The pH of a stock solution of Aureomycin in unbuffered nutrient broth was adjusted to 6.2, 7.0, and 7.8, respectively, and a series of twofold dilutions of each of these three stock solutions was prepared with broth of the corresponding pH. (The bacterial titer was found to be the same at pH 7.0 in both buffered and unbuffered nutrient broth.) Ten strains, which could grow readily at these various pH's, were tested.

In all instances, the most potent antibacterial action of Aureomycin was exhibited at pH 6.2 (Table III). This is a true pH effect on the drug and is

not due to a different rate of bacterial growth at these different pH values, because the controls showed approximately the same number of bacteria after twenty-four hours at all three pH values.

TABLE III. INFLUENCE OF PH ON RESULT OF TEST

SAMPLE STRAINS	pH	CONCENTRATION OF AUREOMYCIN IN LAST CLEAR TUBE (MICROGRAMS PER MILLILITER)	
		AFTER TWENTY-FOUR HOURS	AFTER FORTY-EIGHT HOURS
Hemolytic *Staphylococcus aureus* (sensitive strain)	6.2	0.8	1.6
	7.0	1.6	3.2
	7.8	25.0	100.0
Pseudomonas (resistant strain)	6.2	25.0	100.0
	7.0	50.0	200.0
	7.8	200.0	>200.0

The action of Aureomycin was considerably weaker at pH 7.8 than at pH 7.0 or 6.2, because the drug deteriorates rapidly in an alkaline solution, even if the stock solution is kept at –4° C.

Influence of the medium: Parallel tests were run in nutrient broth (Difco), trypsinized broth, tryptone broth, beef-heart broth, 1 per cent dextrose broth, 5 per cent serum broth, and 10 per cent horse-blood broth, all at pH 7.

The results (Table IV) show that the richer media interfere with the antibacterial action of Aureomycin. The last clear tube after twenty-four hours shifted to the left from one to as many as four tubes. These results confirm similar findings by Bliss and Chandler[2] and by Beigelman.[5]

TABLE IV. BACTERIOSTATIC CONCENTRATION (MICROGRAMS PER MILLILITER) OF AUREOMYCIN IN DIFFERENT MEDIA

SAMPLE STRAINS	NUTRIENT BROTH	TRYPTONE BROTH	BEEF-HEART BROTH (NO PEPTONE)	TRYPSINIZED BEEF-HEART BROTH	1 PER CENT DEXTROSE BROTH	5 PER CENT SERUM (HORSE OR RABBIT) IN NUTRIENT BROTH	10 PER CENT BLOOD BROTH
Hemolytic *Staphylococcus aureus*	0.05-0.1*	0.2-3.2	0.2-6.2	3.2-50	6.25-50	6.25-50	12.5-50
Aerobacter aerogenes	0.8-6.25	1.6-25	3.2-25	12.5-100	12.5-100	25-100	25-200
Proteus vulgaris	3.2-25	6.25-25	12.5-50	50-200	25-100	25-200	50-200
Klebsiella pneumoniae	25-100	50-200	50-200	50-200	100-200	200-200	200-200
Pseudomonas	3.2-6.25	12.5-50	12.5-50	6.25-50	12.5-25	12.5-100	50-200

*The first of each pair of numbers indicates the concentration of Aureomycin in the last clear tube after twenty-four hours; the second, after forty-eight hours.

Tryptose broth interferes least, serum and dextrose broth much more, and blood broth most with the action of Aureomycin. Hence, the sensitivity values obtained by an in vitro test for the effect of Aureomycin on a given strain depends on the medium in which the test is performed. By the method described, the drug is most potent in nutrient broth (Difco).

Correlation Between in Vitro Sensitivity and Clinical Effect of Aureomycin.—

Bacteriologic response: Table V records the findings from a series of 190 patients. The data demonstrate that there is a good correlation between the in vitro sensitivity and the clinical antibacterial effect of Aureomycin. Of 132 strains found sensitive by this method, all but five were eliminated. Of eight borderline strains two were eliminated. None of 124 resistant strains was eliminated. These data are based on cultural data obtained during therapy with Aureomycin and again, in most instances, one to three days after it was discontinued.*

TABLE V. CORRELATION OF IN VITRO SENSITIVITY TEST TO THE CLINICAL BACTERIOLOGIC RESPONSE

		INFECTIONS DUE TO ONE BACTERIAL STRAIN			INFECTIONS DUE TO TWO OR MORE BACTERIAL STRAINS		
DIAGNOSIS	TOTAL NUMBER OF CASES	IN VITRO SENSITIVITY OF RESPONSIBLE STRAIN	NUMBER OF CASES	BACTERIOLOGIC RESPONSE TO AUREOMYCIN	IN VITRO SENSITIVITY OF RESPONSIBLE STRAIN	NUMBER OF CASES	BACTERIOLOGIC RESPONSE TO AUREOMYCIN
Wound infections	62	Sensitive	1	Eliminated	All sensitive	17	All eliminated
		Borderline	1	Not eliminated	Sensitive and resistant mixed	32	31 of 32 sensitive eliminated; all resistant not eliminated
		Resistant	1	Not eliminated	All resistant	10	None eliminated
Urinary tract infections	128	Sensitive	22	21 eliminated; 1 not eliminated	All sensitive	18	17 eliminated
		Borderline	7	2 eliminated; 5 not eliminated	Sensitive and resistant mixed	42	40 of 42 sensitive eliminated; all resistant not eliminated
		Resistant	17	None eliminated	All resistant	22	None eliminated

Clinical response: When there was no complicating pathology, a satisfactory antibacterial effect was followed by rapid disappearance of the clinical evidence of infection. With rare exceptions, the infection did not recur during the patient's hospital stay. When there was complicating pathology, an antibacterial effect either was not secured even with sensitive bacteria or, if secured, was frequently followed by recurrence until complicating pathology was eliminated.

Of 245 patients treated with Aureomycin, 137 were free of complicating pathology before or at the time the antibiotic treatment was started (Table VI). In 53 the infection was due to one or more sensitive strains and in 51 it was rapidly cured. In 5 the infection was due to strains of borderline sensitivity. Only one satisfactory response was achieved by Aureomycin. In

*The dose of Aureomycin, given as the glycinate, varied from 1½ to 3 Gm. daily, averaging 2 Gm. When given intravenously, the dose was 500 mg. twice a day. The route of administration depended principally on presence or absence of nausea or of vomiting. The oral route was always preferred. Treatment was continued for seven to ten days. Cases in which treatment was discontinued earlier are not included in this paper. When treatment for seven to ten days failed, the case was considered and classified as not cured.

23 the infection was due to resistant strains only; none responded to Aureomycin. In 31 the infection was due to a mixture of sensitive and resistant strains; none of these responded to Aureomycin. However, in an additional 25 patients with diffuse peritonitis, caused by a mixture of sensitive and resistant organisms, the cure of the infection was achieved. The sensitive strains were rapidly eliminated. But Pseudomonas or Proteus, or both, which were the resistant strains in all cases, did not disappear in response to Aureomycin. Nevertheless, these strains appeared not to interfere with control of the infection. This observation was also made in experimental peritonitis in the dog.[6]

TABLE VI. CORRELATION OF IN VITRO SENSITIVITY TO THE CLINICAL RESPONSE*

		INFECTIONS DUE TO ONE BACTERIAL STRAIN			INFECTIONS DUE TO TWO OR MORE BACTERIAL STRAINS		
DIAGNOSIS	TOTAL NUMBER OF CASES	IN VITRO SENSITIVITY OF RESPONSIBLE STRAIN	NUMBER OF CASES	RESPONSE	IN VITRO SENSITIVITY OF RESPONSIBLE STRAIN	NUMBER OF CASES	RESPONSE
Wound infections	42	Sensitive	1	Cured	All sensitive	12	11 cured; 1 not cured
		Borderline	1	Not cured	Sensitive and resistant mixed	22	Not cured
		Resistant	1	Not cured	All resistant	5	Not cured
Urinary tract infections	60	Sensitive	18	Cured	All sensitive	12	11 cured; 1 not cured
		Borderline	4	1 cured; 3 not cured	Sensitive and resistant mixed	9	Not cured
		Resistant	10	Not cured	All resistant	7	Not cured
Biliary tract infections	7	Sensitive	2	Cured	All sensitive	5	Cured
		Borderline	-	-	Sensitive and resistant mixed	-	-
		Resistant	-	-	All resistant	-	-
Peritonitis	28	Sensitive	-	-	All sensitive	3	Cured
		Borderline	-	-	Sensitive and resistant mixed	25	Cured†
		Resistant	-	-	All resistant	-	-

*Complicating pathology was absent or had been eradicated in all these patients.

†Peritonitis appears to be the exception to the rule that cure does not result in mixed infections due to resistant as well as sensitive bacteria. The resistant strains were *Bacillus proteus vulgaris* or Pseudomonas or both.

Needless to say, patients with resistant strains who did not respond to Aureomycin frequently improved subsequently because of the effect of other chemotherapeutic agents, surgery, or natural defense mechanism.

DISCUSSION

This study deals exclusively with the relationship of the in vitro sensitivity of the bacteria responsible for the disease to the bacteriologic and clinical response of the patient during and shortly after treatment with the drug. Most patients who responded to the drug were permanently cured. In some cases, especially urinary infections, in which there was a good response to the drug, there was recurrence or reinfection, especially if accompanying pathology had not been dealt with successfully. Others, which were resistant to

Aureomycin, responded to other antibiotics or to surgery, or recovered because of their own defense mechanisms. Since most patients showed some clinical improvement during treatment, even if the bacteria were resistant to Aureomycin,[14] such improvement cannot be attributed to specific drug action, but there are no cases in the series reported here in which bacteria resistant to Aureomycin disappeared during the period of treatment with Aureomycin. That this can and does happen, however, is well known. Even so, the method described provides a reliable index of the clinical response which may be expected from therapy with Aureomycin. A similar method has also proved valid for the sulfonamides.[7] Our data for such a method for penicillin and neomycin, although meager, suggest that the same may prove to be true for these antibiotics as well.

The in vitro titers indicating clinical antibacterial effectiveness are very different for the various drugs. The method described is not the only one that might prove satisfactory.* The clinical validity of this method, or any other, is not established until experience demonstrates a close correspondence between the clinical response and the antibacterial titer.† If such a correspondence is found to hold for a large variety of species, and for many strains within a species, the clinical antibacterial effectiveness of the antibiotic for any given strain will be predictable from the in vitro antibacterial titer alone. For Aureomycin this is 6.2 μg per milliliter or less. Similar data are needed for the other antibacterial agents. A judgment as to the comparative clinical value of different chemotherapeutic agents against a given infecting organism cannot as yet be made by the same test until the correlation between clinical response and in vitro antibacterial concentrations is known for all the agents under consideration.

Jackson and Finland[4] stated that in vitro tests have limited clinical usefulness because of the varying quantitative results of differing techniques. Even with a given technique they obtained a fourfold difference between maximum and minimum values on repeated tests of the same organism. In some 4 per cent of the 350 strains tested with Aureomycin, we found a twofold difference, but the remainder showed no difference on repeat test.

For therapeutic purposes they suggested that it is usually necessary only to identify the causative organism and to dispense with in vitro tests in the case of uniformly sensitive bacteria, that is, Pneumococci or Group A hemolytic Streptococci. In the case of other species, whose susceptibility to the available antibiotics cannot be predicted, they regard the in vitro tests of value. Our data, listed in Table VII, agree with this judgment, for many strains of many species generally considered sensitive to Aureomycin are frequently, in fact, resistant, while some strains of species generally considered resistant are,

*Howe[3] in comparing an agar-plate-disk method with a nutrient-broth method stated that the concentration of Aureomycin required to inhibit growth on the plate is twice as high as that required in broth.

†The disk or tablet method, although very simple, carries a 25 per cent error, according to Spaulding.[9] (This is because the zone of inhibition varies with the medium used, and because the speed of release of the antibiotic to the surface of the plate varies with the surface moisture.) Braude and Dockrill[10] stated in a recent paper that, especially with Aureomycin, the disk method is far inferior to the tube dilution method.

in fact, sensitive. Since a very large percentage of clinical infections are due to strains with unpredictable sensitivity, an in vitro test, such as the one herein reported for Aureomycin, can be used to great advantage in the selection of the appropriate antibiotic. It is obvious that no single test can suffice for all bacteria. Thus the bacilli of tularemia, pertussis, and influenza, as well as other fastidious bacteria, cannot be tested in a simple medium like nutrient broth. Eisenberg and Wagner[11] obtained results similar to ours for a series of antibiotics including Aureomycin in a large series of cases, using a standardized paper-disk method. In a large number of urinary infections, Metzger and associates[12] observed a close correlation between clinical response and antibacterial titer of Aureomycin in vitro. Reiss and co-workers[13] also stated that the in vitro sensitivity test is the most reliable guide for selecting an antibiotic for a given infection.

TABLE VII. SENSITIVITY OF VARIOUS STRAINS WITHIN A BACTERIAL SPECIES TO AUREOMYCIN (LAST CLEAR TUBE AFTER TWENTY-FOUR HOURS)

SPECIES	NUBMER OF STRAINS TESTED	RESISTANT (200 TO 50 μG PER MILLILITER)	BORDERLINE (25 TO 12.5 μG PER MILLILITER)	SENSITIVE (6.25 OR LESS μG PER MILLILITER)
Beta streptococcus Group A	10	-	-	10
Alpha streptococcus	10	3	3	4
Gamma streptococcus	10	2	3	5
Streptococcus faecalis	10	7	1	2
Pneumococcus	10	-	-	10
Hemolytic *Staphylococcus aureus*	20	2	4	14
Nonhemolytic *Staphylococcus aureus*	10	3	3	4
Hemolytic *Staphylococcus albus*	15	8	4	3
Nonhemolytic *Staphylococcus albus*	15	5	5	5
Salmonella typhi	10	-	2	8
Salmonella paratyphi	2	-	-	2
Salmonella schottmuelleri and *Salmonella enteritidis*	8	2	4	2
Various Shigellae	10	1	2	7
Escherichia coli	50	5	5	40
Aerobacter aerogenes	50	13	5	32
Klebsiella pneumoniae	10	5	1	4
Pseudomonas	50	22	16	12
Proteus	50	15	15	20

The method herein described can be simplified for practical clinical purposes by setting up, in place of sixteen tubes, only six, one control tube and five tubes with Aureomycin in concentrations from 50 to 3.2 μg per milliliter.

CONCLUSIONS

1. A standardized twofold serial dilution method for testing sensitivity of bacteria to Aureomycin is described. With this method the clinical antibacterial effectivenes of Aureomycin against the infecting bacteria can be predicted.

2. From the data at hand it appears that if there is no visible growth in vitro after twenty-four hours in an Aureomycin concentration of 6.2 μg per milliliter or less, the bacteria should be eliminated, provided complicating pathology is not present or has been eliminated. If this concentration is between

12.5 or 25.0 μg per milliliter, the clinical affect will probably be a failure. If it is 50 μg per milliliter or higher, the bacteria will almost certainly not be eliminated by Aureomycin.

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THE MANAGEMENT OF PERFORATING INJURIES OF THE COLON AND RECTUM IN CIVILIAN PRACTICE

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THIS report is based on an analysis of forty-two cases of penetrating wounds of the colon and rectum treated in the Shreveport Charity Hospital from January, 1948, to January, 1953, inclusive. The structural outline of this report, for purposes of comparison, is very similar to a report by Woodhall and Ochsner,[1] who reviewed fifty-five cases of patients with perforating wounds of the colon and rectum admitted to the Charity Hospital in New Orleans from 1944 to 1948, inclusive.

Prior to their report, Imes[2] was singular in recommending primary suture with enthusiasm. Woodhall and Ochsner's report also pointed out the profound influence that the writings of Ogilvie,[3] Morgan,[4] Mason,[5] Hurt,[6] Hamilton,[7] Colcock,[8] and Taylor and Thompson,[9] dealing with the treatment of colon lesions in combat wounds, had on the treatment of colon and rectal wounds in civilian practice. Woodhall and Ochsner suggested that this influence of the writings of the World War II surgeons may have overemphasized the principle of exteriorization of all wounds of the colon and rectum. With the continuous development of newer and improved antibiotics, better pre- and postoperative care, and early definitive treatment, a critical analysis of the methods of treatment is warranted. This report further suggests that in selected cases with early definitive treatment more wounds can be closed primarily with safety and with the resultant decrease in the number of operations and in economic loss to the patient.

Mortality.—The mortality rates from traumatic injuries of the colon and rectum generally have been high regardless of the type of therapy. Quite consistently, those obtained in civilian practice have been higher than those obtained in battle injury (Table I).

In the present series of 42 patients operated upon, 6 died (14.3 per cent). Although a mortality rate of 14.3 per cent is high, it is considerably lower than those reported both in civilian and military practice (Table I).

TABLE I. MORTALITY RATES IN COLON AND RECTAL WOUNDS

SOURCE	YEAR REPORTED	MORTALITY RATE (PER CENT)	
Present series	1953	14.3	Civilian
Woodhall and Ochsner	1949	20	
Taylor and Thompson	1948	27	Military
Imes	1945	26	
Hurt	1945	33	
Ogilvie	1944	53	
Wilkinson, Hill, and Wright	1946	79.3	Civilian
Elkin and Ward	1943	53	
Rippey	1941	62.5	

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Incidence.—

Age: The average age in the present series was 34.8 years, whereas in the fatal cases it was 34.1 years. Generally the prognosis is poorer in the older person because of degenerative conditions.

Sex: Of the 42 patients, 29 (69.1 per cent) were men and 13 (30.9 per cent) were women. The mortality rate for men was 10.34 per cent and for women 23.07 per cent.

Race: Thirty-five patients (83.33 per cent) were Negroes and 7 (16.66 per cent) were white. The mortality rate for Negroes was 14.3 per cent and for whites it was 14.2 per cent.

Mechanism of Injury.—The mechanism by which the injury occurred varies considerably from single gunshot injuries, multiple gunshot injuries, shotgun blasts, stabs, instrumentation, and falls to auto accident (Table II).

TABLE II. INJURING MECHANISM IN FORTY-TWO CASES

CAUSE	NUMBER	DEAD	MORTALITY (PER CENT)
Gunshot	20	0	0
Multiple gunshot	3	0	0
Stab	5	1	20.0
Shotgun	5	4	80.0
Instrumentation	7	1	14.3
Auto accident	1	0	0
Unknown	1	0	0
Total	42	6	

Single gunshot wounds formed almost one-half of the injuries in the present series and were associated with no mortality. Tearing and mangling of the intra-abdominal viscera are less likely with this type of injury.

The mortality rate of stab wounds was 20.0 per cent, and shotgun blasts of the colon carried a mortality of 80.0 per cent in this series, thus illustrating the seriousness of stab wounds and shotgun blasts.

Shock.—The presence of shock in the patient when first seen and its persistence up to the time of operation are of great prognostic value (Table III).

The mortality rate in patients first seen in shock was 23.07 per cent, and in cases when shock persisted up to time of operation it was 75.0 per cent.

TABLE III. SHOCK

	NUMBER	DEAD	PER CENT
Before surgery	13	3	23.07
On arrival at operating room	4	3	75.0

It is likely that more than 13 of these patients were in shock before surgery, since the information was frequently omitted from the admitting record.

Of the 4 patients in whom adequate therapy was employed unsuccessfully and who were sent to the operating room in shock, 3 died (75 per cent).

Time Lag.—The longer the time elapsing from injury to institution of the therapy, the worse the prognosis (Table IV). The mortality rate in the group

TABLE IV. TIME LAG

LAG (HOURS)	NUMBER OF CASES	DEAD	MORTALITY (PER CENT)
0-3	18	1	5.5
3-6	10	2	20.0
6-9	5	1	20.0
9-12	1	0	0.0
12-18	1	0	0.0
18-24	1	1	100.0
24-48	3	0	0.0
48-72	2	1	50.0
10 days	1	0	0.0
Total	42	6	

treated within the first three hours was markedly below the over-all mortality rate. In civilian practice, most patients arrive shortly after injury.

The greater the lag period, the fewer the patients who will survive to reach the hospital. The earlier the casualty is admitted to the hospital, the sooner shock can be treated and the patient prepared for operation. Antibiotics and chemotherapy have reduced much of the danger of delay and resulting peritonitis.

Mortality of Wounds.—Injury to other intra-abdominal viscera in addition to the colon increases the mortality rate considerably (Table V).

TABLE V. WOUNDS

SERIES AND ORGAN INVOLVED	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
Present series			
Multiple organs	28	5	17.8
Large intestine alone	14	1	7.1
Woodhall and Ochsner			
Multiple organs	32	9	28.1
Large intestine alone	23	2	8.7
Taylor and Thompson			
Multiple organs	39	12	31.0
Large intestine alone	28	5	18.0

Of the 42 patients in the present series 28 (66.6 per cent) had injuries to other intra-abdominal viscera aside from the colon. The other organs injured were: liver (3 cases), stomach (1 case), kidney (3 cases), spleen (2 cases), small bowel (21 cases), bladder (2 cases), chest and ribs (5 cases), diaphragm (2 cases), urethra (1 case), uterus (1 case), sacral plexus (1 case), external iliac vessels (1 case), spermatic vessel (1 case), bony pelvis (2 cases), gastrocolic ligament (2 cases), suspensory ligament (1 case), buttocks (1 case), and deltoid muscle (1 case).

The low mortality rate in cases when only the colon is injured is indeed striking. This reflects the minor nature of some of the perforations, lack of massive fecal contamination, employment of adequate surgery, and control of peritonitis.

Site of Colon Injury.—Injuries of the right colon and sigmoid and rectosigmoid carried a grave prognosis in this series (Table VI). Injuries of the ascending and descending colon are more likely to be single and therefore asso-

ciated with a lower mortality rate. Injuries of the transverse colon, because of its relatively central position in the abdomen, generally are accompanied by injuries to other intra-abdominal organs and as a rule cause a high mortality rate; however, this was not reflected in this series. It is of interest that injuries of the extraperitoneal rectum caused no fatalities.

TABLE VI.

SITE OF INJURY	NUMBER OF CASES	DEATHS	
		NUMBER	PER CENT
Right colon	8	3	37.5
Transverse colon	6	0	0
Splenic flexure and descending colon	9	1	11.1
Sigmoid and rectosigmoid	13	2	15.3
Extraperitoneal rectum	6	0	0
Total	42	6	

Methods of Treatment.—In the present series a number of methods were used to treat perforated injuries of the colon and rectum (Table VII).

TABLE VII. METHODS OF TREATMENT

METHOD	NUMBER	DEAD	
		NUMBER	PER CENT
1. Primary suture	17	0	0
2. Primary suture with proximal decompression	6	1	16.6
3. Exteriorization	10	2	20.0
4. Resection with exteriorization	2	1	50.0
5. Resection with primary anastomosis	3	2	66.6
6. Proximal decompression with incision and drainage of perineum (rectum)	4	0	0
Totals	42	6	14.3

1. *Analysis of primary suture:* Of 17 patients there were no deaths. The average hospitalization was 11.8 days. Complications were one wound abscess.

2. *Analysis of primary suture with proximal decompression:* Of 6 patients there was one death (16.6 per cent mortality). The average hospitalization was 65.0 days. Complications were one case of evisceration.

3. *Analysis of exteriorizations:* Of 10 patients there were two deaths (20.0 per cent mortality). The average hospitalization was 48.3 days. Complications were two wound abscesses and one case of evisceration.

4. *Analysis of resection and exteriorization:* Of 2 patients there was one death (50 per cent mortality). The average hospitalization was 144.0 days. Complications were phlebothrombosis with pulmonary embolism. This patient made a complete recovery.

The one death when resection and exteriorization were used occurred in one of the patients taken to the operating room in shock. The traumatic lesions consisted of massive mangling and perforations of the terminal ileum, ascending colon, and hepatic flexture due to a shotgun blast. There was massive

hemorrhage from a tear in the superior mesenteric vein and marked retroperitoneal hemorrhage around the right kidney and ureter. An intra-arterial transfusion was necessary using the radial artery. This patient died from irreversible shock and delayed hemorrhage twenty-eight hours after surgery.

5. *Analysis of resection and primary anastomosis:* Of the 42 patients with colon wounds 3 were treated by resection of the traumatized bowel followed by primary anastomosis with two deaths (66.6 per cent mortality). In the patient who survived there was one complication of a fecal fistula of the small bowel, which closed spontaneously in approximately three weeks. The average hospitalization was thirty-one days.

In one of the fatal cases, the patient died on the sixteenth postoperative day from a lower nephron syndrome and peritonitis. This patient received a shotgun blast of the ascending colon and hepatic flexure.

In the second case, the patient died on the sixteenth postoperative day because of delayed hemorrhage from the liver. This patient received a shotgun blast of the right lobe of the liver, terminal ileum, ascending colon, and hepatic flexure. On the seventh day after surgery, the wound of the point of entry broke down, and later massive delayed hemorrhage from the liver occurred on the day of death.

6. *Analysis of extraperitoneal rectal wounds:* There were 6 patients with extraperitoneal rectal wounds, and all recovered. Four patients had sigmoid colostomy with or without drainage of the rectal wound by incision through the perineum. Two patients had primary suture of the rectum performed immediately following laceration of the rectum which inadvertently occurred during colpotomy for a cul-de-sac abscess and a perineal prostatectomy.

TABLE VIII. ANALYSIS OF CASES AND DEATHS BY YEARS

YEAR	NUMBER OF CASES	DEATHS	
		NUMBER	PER CENT
1948	10	1	10.0
1949	1	0	0
1950	11	3	27.2
1951	7	1	14.2
1952	13	1	7.6

Days of Disability.—

1. *Analysis of primary suture:* From the injury to discharge the average hospitalization was 11.8 days (Tables IX).

TABLE IX. DAYS OF DISABILITY

	METHODS OF TREATMENT		
	Primary suture	Resection with primary anastomosis	1. Proximal decompresion with or without primary suture (secondary closure of colostomy) 2. Exteriorizations and colostomies (secondary closure of colostomy) 3. Resection with exteriorization (secondary closure of colostomy)
Time from injury to discharge	11.8 days	31.0 days	58.2 days

2. *Analysis of resection with primary anastomosis:* From the injury to discharge the average hospitalization was 31.0 days.

3. *Analysis of proximal decompression with or without primary suture, exteriorizations and colostomies, resections with exteriorizations, all methods of treatment being followed by closure of colostomy:* From injury to discharge the average period of disability was 58.2 days.

Preoperative Treatment.—The patient is usually brought to the emergency admitting room within six hours of injury (twenty-eight of forty-two cases). Shock is generally the rule, depending on the extent of the injury. If the blood pressure is unobtainable, 0 negative blood is rapidly transfused intravenously and/or intra-arterially. If the shock is not so severe, the patient is typed and matched for blood, nasal oxygen is administered, and portable x-ray pictures of the abdomen and chest are made without moving the patient. Tetanus antitoxin, penicillin, streptomycin, and, in the last two years, intravenous Aureomycin or terramycin are administered.

The majority recover rapidly from shock. Premedication is then given and surgery is performed immediately. A Levin tube is inserted into the stomach and alcohol and food particles are aspirated when present. Four patients in this series did not recover from shock under this management, and it was necessary to perform surgery with the patient in shock with a resultant 75 per cent mortality.

Operative Treatment.—Endotracheal anesthesia with gas-oxygen-ether mixtures is administered. As a rule most of the patients have alcoholic beverages and food particles in the stomach. The anesthetist is instructed to aspirate the Levin tube frequently and allow it to drain throughout the procedure.

A long paramedian incision is employed as a rule. Hemorrhage is first controlled, and perforations of the colon are closed temporarily while a search is made for damage in the small bowel and stomach.

Types of Repair.—Primary closure was employed in seventeen cases with 0 per cent mortality. Primary closure was not employed in any wound in this series which was over six hours old at the time of surgery. This type of closure was employed in single and multiple wounds of the colon and rectum, where it was judged by the operator that a good two-layer closure with viable edges could be obtained without compromising the lumen of the bowel.

Lesions of the extraperitoneal rectum as a rule were not closed. Perineal drainage was employed with a proximal sigmoid colostomy. However, two of six perforations of the extraperitoneal rectum in this series were closed primarily with perineal drainage. One case occurred during a perineal prostatectomy and one occurred during drainage of a cul-de-sac abscess. Both were recognized at the time and were immediately closed in layers.

Shotgun wounds present our most serious problem. Four patients in this series sustained shotgun blasts at close range, which mangled and destroyed the right colon with multiple associated injuries of other abdominal viscera. In three cases the right colon was resected with primary anastomosis of the ileum

to the transverse colon. One case of a Mikulicz type ileotransverse colostomy was exteriorized. The shotgun-type lesion carried an 80 per cent mortality.

Many of the twenty-three cases that were exteriorized or closed with proximal decompression were lesions that were small and seen within the first six hours of injury and which could, in retrospect, have been closed primarily without additional risk to the patient.

The abdomen is closed in layers with chromic 0 suture on the peritoneum and interrupted cotton sutures on the fascia and skin. Retention sutures of Dermalon or stainless steel are employed in most cases to help prevent wound dehiscence. Drainage is routinely employed by bringing a rubber drain through a stab wound in the flank.

Postoperative Treatment.—Levin tubes connected to a suction apparatus are routinely employed until bowel sounds are present and flatus is passed per rectum or per colostomy. Streptomycin and penicillin were given routinely from 1948 through 1950, and since 1950 intravenous Aureomycin or terramycin has been employed until the patient is placed on oral feeding, at which time Aureomycin or terramycin is given by mouth.

SUMMARY

A series of forty-two cases of perforating injuries of the colon and rectum with a 14.3 per cent mortality has been reviewed. This comparatively low mortality rate is attributed in part to the increased use of streptomycin, Aureomycin, and terramycin.

Seventeen cases with single or multiple perforations of the colon and rectum were closed primarily with no mortality. This group was comprised, in the greater part, of wounds not over two inches in diameter and which received definitive treatment within six hours of injury. Primary closure in wounds of this type has in this series proved to be a safe procedure.

Primary suture with proximal decompression was employed in six cases with 16.6 per cent mortality. In most of these cases the injuries were in the relatively fixed portion of the colon or rectum.

Exteriorization was employed in ten cases with a 20 per cent mortality. Of this group, those patients who had small wounds and were treated early could have been treated by primary suture with reduction in morbidity and less loss of time.

In two cases, resection with exteriorization was employed with a 50 per cent mortality rate, and in three cases resection with primary anastomosis was performed with 66.6 per cent mortality. The high mortality in this group was primarily the result of severe initial injury with multiple gunshot involving multiple abdominal organs.

In six lesions of the extraperitoneal rectum two were closed primarily without proximal decompression. Four had proximal decompression. All had perineal drainage with no mortality.

So markedly has the use of the more recent antibiotics improved the prognosis of colon wounds that primary closure in selected cases is the preferred procedure.

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THE ASSOCIATION OF LYMPHOGRANULOMA INGUINALE AND CANCER

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ELEVEN cases in which lymphogranuloma inguinale apparently predisposed to neoplastic degeneration are reported in this paper. Only in recent years has it been suggested that there may be an association between lymphogranuloma inguinale and cancer. In 1935, Coutts[1] reported a case of round-cell sarcoma developing on a rectal stricture in a 15-year-old boy who had been a passive pederast. The Frei test was positive. Coutts was the first author to suggest that lymphogranuloma inguinale predisposed to malignancy, especially in view of the rarity of sarcoma of the rectum.

Liccione,[2] in 1936, was the first to describe rectal adenocarcinoma complicating lymphogranuloma inguinale. Two cases of adenocarcinoma of the rectum were described. In one, the patient had a rectal stricture with associated fistulas. After two years a Frei test was positive and biopsies of the stricture showed no neoplastic disease. A colostomy was performed, and one year later rectal adenocarcinoma was discovered. The second patient had a rectal stricture with fistulas for fifteen years after which time adenocarcinoma was discovered at the site of the stricture. Although no Frei test had been performed, the chronicity of the anorectal disease and elephantiasis of the vulvar and ischiorectal skin offered presumptive evidence of lymphogranuloma inguinale.

The same year, Lisa[3] described the autopsy findings in a Negro woman who had had a rectal stricture of two years' duration with a positive Frei test. Autopsy findings included: adenocarcinoma of the pelvic colon, squamous-cell carcinoma of the anal canal, and tuberculosis of the femoral, inguinal, and iliac nodes.

David and Loring,[4] in 1939, reported three cases of squamous-cell carcinoma of the rectum, associated with the chronic anorectal manifestation of lymphogranuloma inguinale. Two patients had positive Frei tests and had had operations diverting the fecal stream, one two years and the other twelve years prior to the detection of carcinoma. Although a Frei test was not performed on the third patient, the chronicity and nature of the rectal stricture suggested lymphogranuloma as an etiology.

The tendency for neoplastic degeneration to occur at sites of prolonged chronic inflammation, such as in cutaneous ulcers and scars of burns, is well

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known. Carcinomatous degeneration has been reported to occur in over 5 per cent of cases of chronic idiopathic ulcerative colitis.[28] Although the relationship of lymphogranuloma inguinale to neoplasia is perhaps less apparent, the incidence has been reported as ranging from less than .1 per cent (Guzman)[5] to 8.6 per cent (Barber and Murphy).[6] It remains debatable whether lymphogranuloma inguinale, per se, or its prolonged inflammatory residual, such as rectal strictures, fistulas, sinuses, and esthiomenes, are the factors predisposing to development of carcinoma.

A survey of the literature disclosed ninety-five patients with lymphogranuloma who subsequently developed carcinoma. Only those cases have been included in which either patients had a positive Frei test or the chronic clinical manifestations of lymphongranuloma inguinale were apparent.[1-27] I am reporting eleven additional cases, one from the Presbyterian Hospital and ten from the Cook County Hospital, Chicago, Ill.

These latter cases were found in the records at Cook County Hospital between 1937 and 1950, during which time 220 cases were diagnosed as strictures of the rectum due to lymphogranuloma inguinale. Of this group, ten patients were found in whom carcinoma was associated with lymphogranuloma inguinale. In these latter patients the diagnoses were confirmed by a positive biopsy for carcinoma and a positive Frei test. The incidence of neoplasia was found to be 4.5 per cent. There were twenty additional cases in which either a biopsy for carcinoma or a Frei test had not been performed to support the clinical diagnoses, and therefore they are not included in this series.

An analysis of the ninety-five cases collected from the literature and of the eleven cases in my series reveals that the majority were in Negro women. In some instances in the literature, the information pertaining to sex and race was not available (Fig. 1).

The sites at which these malignancies developed are shown in Fig. 2.

The intradermal Frei test was positive in seventy-three of the cases collected from the literature and in all of the eleven cases which I am reporting. The results of the Frei test were not stated in twenty-two of the cases found in the literature. However, as previously stated, all of these latter patients had the residual manifestations compatible with a diagnosis of lymphogranuloma inguinale. In five instances, two of these cases being in my series, a previously positive Frei test had reverted to negative at the time of carcinomatous degeneration (Fig. 3).[11, 15]

An analysis of the age distribution of these patients at the time of detection of cancer reveals that the majority were in the younger age groups, between the years of 31 and 50. In some instances this information was not available in the literature (Fig. 4).

In twenty-five cases the clear-cut relationship between carcinoma and lymphogranuloma inguinale was complicated by the presence of one or more of the following accompanying diseases: syphilis (20), chancroid (12), granuloma inguinale (6), and rectal tuberculosis (3). Sixteen of the twenty-five patients had two or more of these diseases. Forty-nine patients with lymphogranuloma

inguinale subsequently developed anorectal neoplasms. The sex, race, and age distribution of this latter group reveals again that the majority were Negro women between the ages of 31 and 50 years (Figs. 5 and 6). In this group of forty-nine patients with anorectal neoplasms complicating lymphogranuloma inguinale a Frei test was positive in thirty-four instances. In the remaining

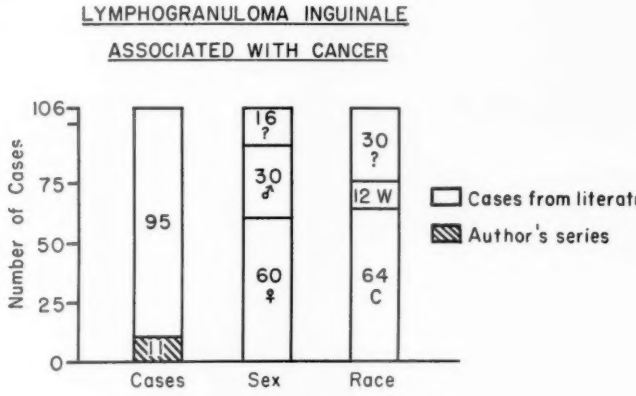


Fig. 1.

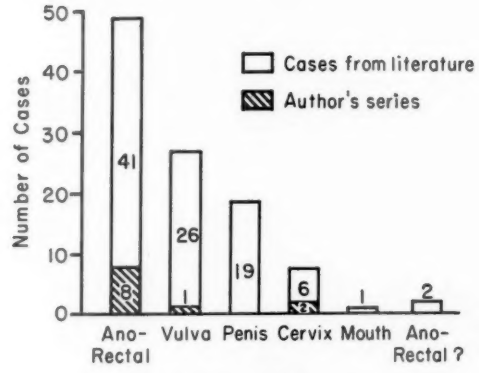


Fig. 2.

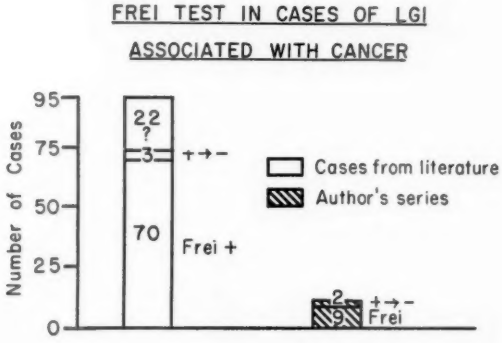


Fig. 3.

Figs. 1-3.

cases these data were not stated in the literature. Anorectal carcinomas were superimposed on a rectal stricture in thirty-one cases; eighteen patients probably had rectal strictures, although this was not stated definitely. Only one of

the group definitely did not have a previous rectal stricture.[26] The duration of the lymphogranulomatous process prior to the detection of anorectal neoplasms was in most instances more than ten years. In twenty-five cases reported in the literature, data concerning the duration of the disease were not available (Fig. 7).

The cell type of the anorectal malignancies complicating lymphogranuloma inguinale is shown in Fig. 8. Apparently, rectal adenocarcinoma complicating

Fig. 4.

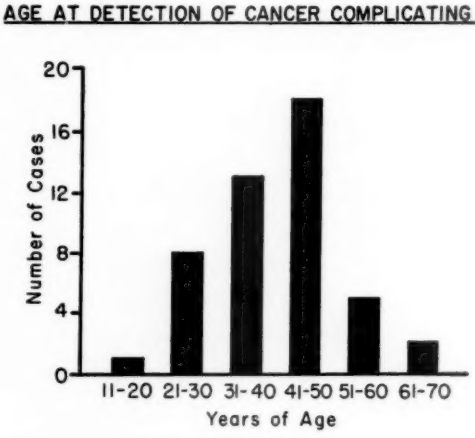


Fig. 5.

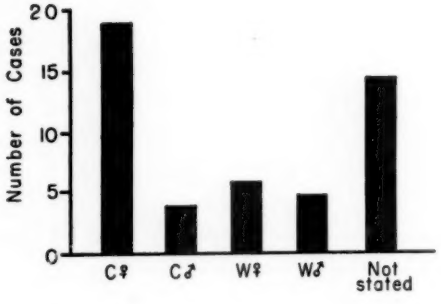
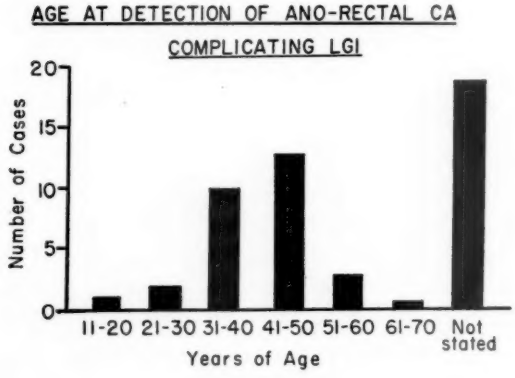


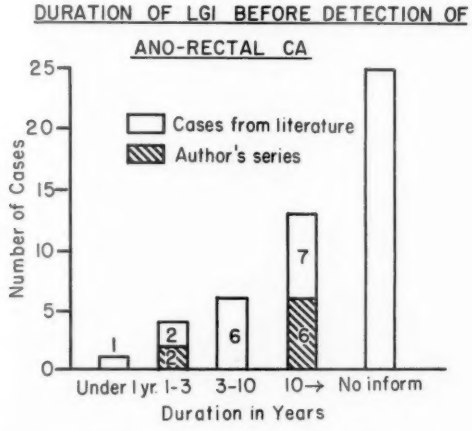
Fig. 6.



Figs. 4-6.

lymphogranuloma inguinale is quite rare, since only seven cases were found in the literature. All these patients had chronic rectal strictures. However, a Frei test was not reported in four of this group.[2, 6, 20] In two other cases, rectal tuberculosis was a complicating factor.[3, 21] In still another case the adenocarcinoma developing in the rectosigmoid may have been coincidental, since the lymphogranulomatous stricture was apparently confined to the rectum.[17]

Fig. 7.



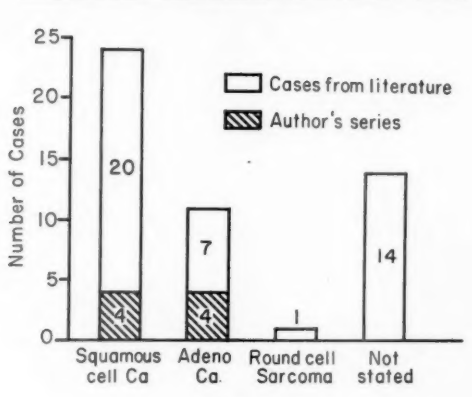


Fig. 8.

I am reporting four additional cases of rectal adenocarcinoma complicating lymphogranuloma inguinale. The following patient, whom I observed at the Presbyterian Hospital of Chicago, is illustrative of this group.

CASE REPORTS

CASE 1.—J. G., a 46-year-old white woman, was first admitted to the Presbyterian Hospital, Chicago, in January, 1939. She then claimed that for the preceding two years she had experienced progressively painful defecation with obstipation and with "pencillike" and frequently blood-streaked stools. In 1938, she had been under the care of a doctor who prescribed mineral oil, cathartics, and enemas, and who dilated the rectum two times a week, with some relief or symptoms. In the week prior to admission she suffered marked rectal

distress with progressive difficulty in defecation. Examination on admission revealed the colon to be distended and palpable in its entire extent. A stricture of the rectum admitting the tip of the index finger was located 3 cm. proximal to the anal ring. The mucosa distal to the stricture was rough and granular, and showed changes typical of those seen in lymphogranuloma inguinale. This impression was confirmed by a positive Frei test. The blood Kahn test was negative. A double-barreled sigmoid colostomy in continuity was performed.* A biopsy of the rectal stricture showed no evidence of malignancy (Fig. 9). Postoperatively, the course was uneventful, and the patient received sulfanilamide for the following year.

The second admission was in April, 1940, at which time the patient was apparently in good health. Examination of the rectum under anesthesia revealed a purulent discharge from the rectum. The stricture, which was just above the mucocutaneous line, could not be probed and was felt by vaginal palpation to be like an indurated cord, extending superiorly to the level of the posterior fornix. A catheter passed distally in the colostomy reached this area but would go no further.

The third admission in May, 1940, was preceded by shifting, cramping abdominal pain and obstipation for one week with failure of the colostomy to function for two days prior to admission. Examination revealed the lumen of the colostomy to be markedly stenosed. This was remedied by revising the afferent stoma.

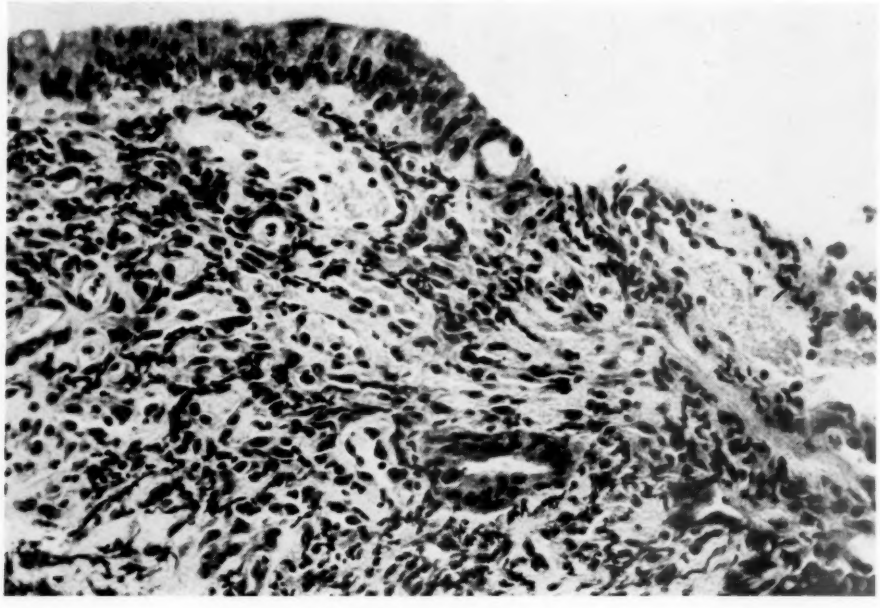


Fig. 9.—Medium-power photomicrograph of a biopsy of the rectal stricture, which was made twelve years before the detection of carcinomatous degeneration. It shows chronic inflammation and fibrosis and an area of mucosal ulceration.

In ensuing years the patient experienced good health and was admitted the fourth time in August, 1944, for consideration of closing the colostomy. However, rectal examination under anesthesia revealed the mucosa at the level of the stricture to be ulcerated and covered with a purulent exudate. Barium-contrast x-ray studies revealed a marked stricture of the rectum involving the distal 10 cm. with an apparently complete obstruction at the proximal end of the stricture (Fig. 10). Consideration of dilating the rectal stricture was therefore abandoned. Examination of the purulent rectal exudate revealed no acid-fast bacilli, and the intradermal Frei test was again positive.

*By Dr. Vernon C. David and Dr. Richard K. Gilchrist, who also performed subsequent operations.

The patient remained in good health until the fifth admission in August, 1950. During the preceding week she had had cramping abdominal pain with poor results from colostomy flushings and had experienced moderate pain in the rectum. This pain was associated with the desire to defecate, and on doing so she would pass bloody purulent material through the anus. Examination on admission revealed a temperature as high as 102.4° F. Vaginal palpation revealed a firm mass, 7 cm. in diameter, in the left perirectal area and about 6 cm. above the anus. The anus would not admit the tip of the little finger, and water from above would barely go through to the anus. The colostomy opening had narrowed. Therefore the colostomy stoma was again revised and the stricture at the anal outlet was dilated, resulting in the evacuation of about 30 c.c. of pus. The mucosa was described as being very red, inflamed, and soft, with nothing that resembled tumor. Ten centimeters above the anus, the rectal stricture was again excessively narrow. A culture of pus from the perirectal abscess revealed predominantly *Streptococcus viridans*, with a minor growth of *Staphylococcus aureus*.

Fig. 10.—Photograph of an x-ray film made of the rectum after a barium enema and introduction of barium into the distal stoma of a sigmoid colostomy. It shows a marked stricture of the distal rectum with an apparent complete obstruction at the proximal end of the stricture. This x-ray picture was made seven years prior to the detection of carcinoma.

Convalescence was uneventful and the patient was able to return to work as a secretary. However, she continued to have an anal discharge of thick yellow pus and small amounts of blood, associated with cramping, lower abdominal pain and night sweats.

In April, 1951, she noted a ten-pound weight loss and progressive malaise, necessitating a sixth admission. Vaginal examination again revealed the rectum to be excessively indurated. Because of the progressively incapacitating course and in view of a suspicion of a superimposed malignancy, an abdominoperineal resection was performed. Abdominal exploration

revealed no pathologic changes. The rectum was mobilized with great difficulty, as it was densely adherent to the sacrococcygeal junction and to the base of the bladder and vagina. About 4 cm. from the anus, a small rectovaginal fistula was observed. The postoperative course was uneventful, with the perineal wound granulating and healing at a normal rate. It

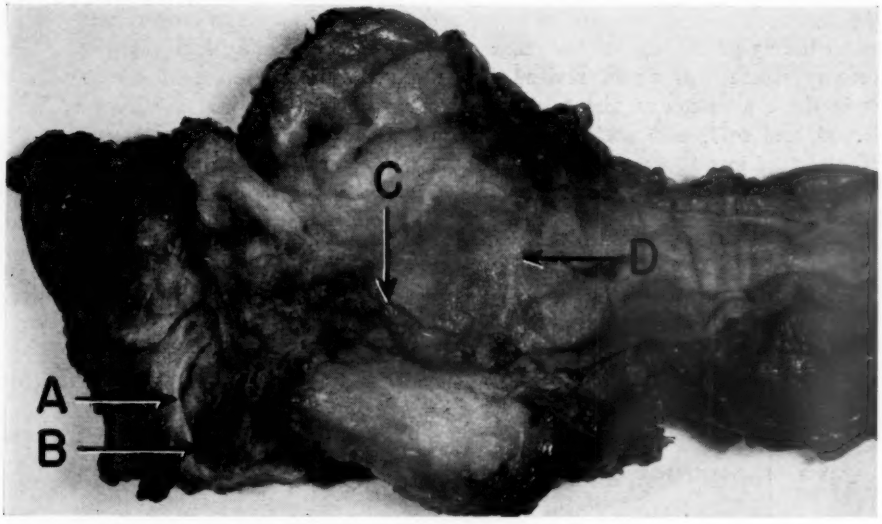


Fig. 11.—Photograph of the surgical specimen from the patient mentioned in the adjoining case report and the preceding two illustrations showing: *A*, squamocolumnar junction, *B*, distal extension of the colloid adenocarcinoma, *C*, proximal extension of the colloid adenocarcinoma, *D*, granular mucosa at the site of the rectal stricture due to lymphogranuloma inguinale.

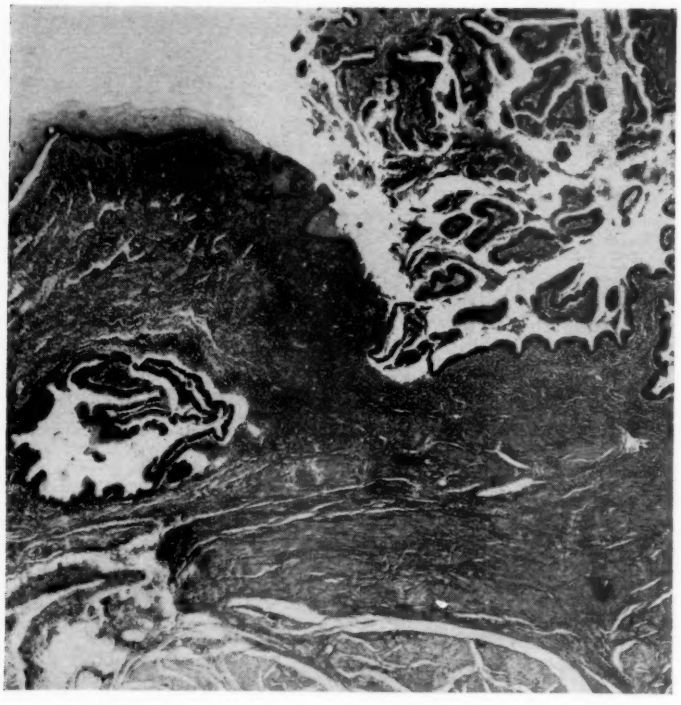


Fig. 12.—Low-power photomicrograph of tissue removed from the previously illustrated surgical specimen showing an adenocarcinoma infiltrating beneath the squamocolumnar junction.

is interesting to note that the intradermal Frei test was repeated preoperatively but resulted in only an area of slight erythema 1.5 cm. in diameter and without induration or elevation. This was interpreted as negative. The Frei test was repeated twice, postoperatively, using

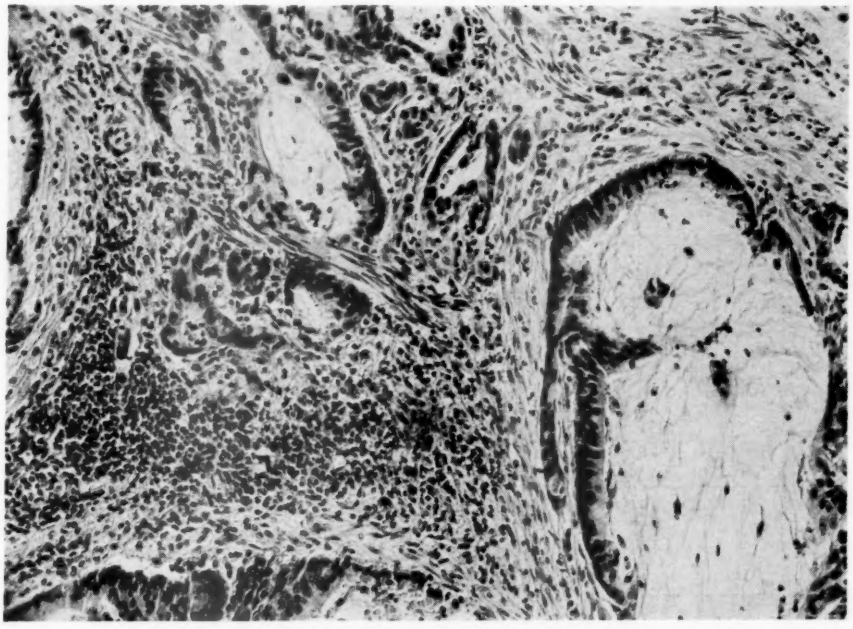


Fig. 13.

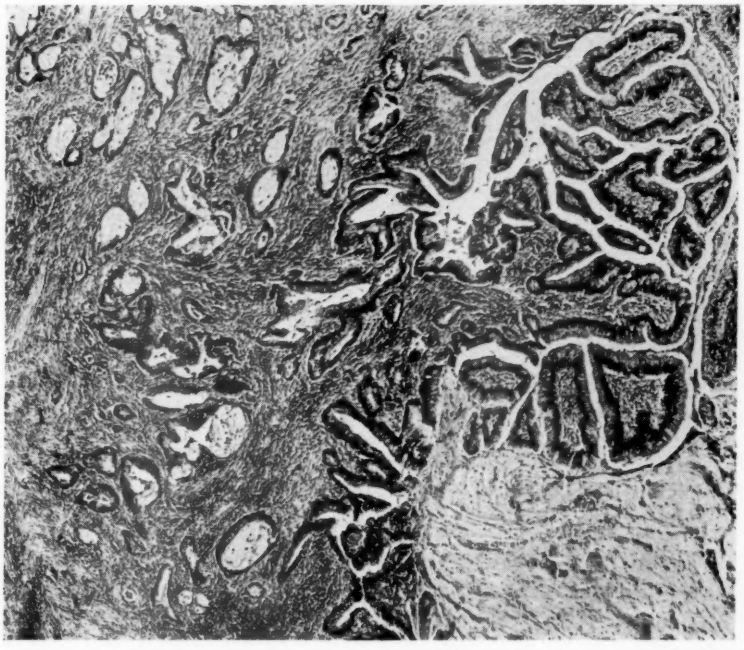


Fig. 14.

Figs. 13 and 14.—High-power photomicrograph of tissue removed from the surgical specimen illustrated in Fig. 11 showing the colloid-producing tendency of this adenocarcinoma with infiltration into the muscular wall of the rectum.

TABLE I*

CASE	SITE	TYPE OF CANCER	CHRONICITY OF LYMPHOGRANULOMA INGUINALE (YEARS)	AGE AT TIME CARCINOMA WAS DETECTED (YEARS)	RACE	SEX	FREI TEST†	BLOOD KAHN TEST†	MISCELLANEOUS DATA
1	Anorectal	Adenocarcinoma	14	45	W	F	P-N		Colostomy 12 yr. prior to detecion of carcinoma
2	Anorectal	Adenocarcinoma	30	50	N	F	P		
3	Anorectal	Adenocarcinoma	14	52	N	F	P		
4	Anorectal	Adenocarcinoma	1	55	N	M	P	P	
5	Anorectal	Squamous-cell carcinoma	24	44	N	F	P	P	Granuloma inguinale
6	Anorectal	Squamous-cell carcinoma	17	48	N	F	P		
7	Anorectal	Squamous-cell carcinoma	12	41	N	M	P	P	Granuloma inguinale (? central nervous system syphilis)
8	Anorectal	Squamous-cell carcinoma	1	45	W	M	P-N		Colostomy 10 mo.
9	Cervix	Squamous-cell carcinoma	18	45	N	F	P		Colostomy 1 yr. prior to detection of carcinoma; pulmonary tuberculosis
10	Cervix	Squamous-cell carcinoma	12	30	W	F	P		Colostomy 4 yr. prior to detection of carcinoma
11	Vulva	Squamous-cell carcinoma	5	32	W	F	P		Vulvar esthiomene; no rectal stricture

*Data from eleven cases of lymphogranuloma inguinale complicated by the development of carcinoma. These previously unreported cases were collected from the Presbyterian Hospital and Cook County Hospital of the City of Chicago.

†P represents positive; P-N represents positive, subsequently becoming negative.

two different commercial antigens and was again negative without erythema or induration. The operative specimen (Fig. 11) was 25 cm. long, with an anal orifice barely admitting the tip of the little finger. One-half centimeter above the pectinate line, a soft, gelatinous, slightly elevated, and polypoid lesion was present, almost completely surrounding the circumference of the bowel and extending proximally for 4 cm. The edges of this lesion in some areas were moderately indurated. The mucosa for 7 cm. proximal to this lesion was rough and granular, the lumen being narrowed to 2 to 3 cm. in diameter. The wall of the rectum in this portion was thickened and surrounded by a moderate amount of excessively indurated perirectal fat. The sigmoid colon and proximal one-third of the rectum were grossly normal. Microscopically (Figs. 12 and 13), the lesion was a colloid adenocarcinoma which had infiltrated deeply in some areas into the musculature of the rectum, but not beyond. The carcinoma extended down to and infiltrated beneath the squamocolumnar junction. In both the carcinoma and the proximal portion of the strictured rectum there were numerous areas of acute and predominantly chronic inflammatory cells. In the entire strictured portion of the rectum, fibroblastic proliferation was excessive and severe perirectal fibrosis was apparent. The mucous membrane over the proximal stenosed portion of the rectum, although not involved by carcinoma, contained atypical glands, the cells of which were well oriented, but larger than normal with hyperchromatic nuclei.

Subsequent examination revealed that in May, 1951, the patient developed a perineal abscess. Biopsy at this site showed recurrent mucus-secreting adenocarcinoma. A local resection of this perineal mass and the posterior vaginal wall was performed in September, 1952. The postoperative course was uneventful.

Information relevant to the remaining ten cases in my series, which were collected from the records at the Cook County Hospital of Chicago, is presented in Table I.

DISCUSSION

A colostomy does not remove the hazard of subsequent carcinomatous degeneration. It is interesting to note that an operation sidetracking the fecal stream, namely, a colostomy, cecostomy, or ileostomy, had been performed in eleven cases at varying intervals prior to the detection of carcinoma (Table II). Nine of these patients subsequently developed anorectal neoplasms; the other two patients had also had colostomies performed, one and four years, respectively, before the discovery of carcinoma of the cervix with infiltration of the rectovaginal septum. There has been little warning in the literature that a colostomy, although relieving the symptoms of a severe rectal stricture and its associated fistulas and abscesses, may not remove the hazard of a complicating carcinoma. In fact, in many of these patients with severe residuals of lymphogranuloma inguinale, a colostomy may temporarily relieve a chronic intestinal obstruction, but fibrobsis, abscesses, and fistulous tracts may persist frequently, with copious amounts of purulent and sometimes sanguineous drainage, in spite of the modern chemotherapeutic agents. In addition, the persistence of the lymphogranulomatous inflammation in some patients is manifested by anemia, amyloid disease, and an extension of the fibrotic granulomatous process, resulting in obliteration of the afferent loop of the colostomy.[29] Therefore, if the inflammatory process persists after proper drug therapy and a defunctioning colostomy, then a combined abdominoperineal resection is indicated. As a result of the latter operation, the greater part of the diseased tissue can be excised and the risk of developing a superimposed anorectal carcinoma is removed. It

must be borne in mind, however, that the mortality rate will be higher with this more extensive operation, since these patients are frequently in a severely debilitated condition; also, the extensive inflammation and fibrosis make the perineal dissection considerably more difficult and time-consuming. Therefore, if the patient's health is complicated by severe inflammation, debilitation, or intestinal obstruction, a single-barreled type of sigmoid colostomy may be performed in which the proximal end is brought out through a stab wound and the distal loop is delivered through the laparotomy incision. This maneuver will facilitate the abdominoperineal resection, which should be performed if the inflammatory process persists after adequate conservative therapy.

TABLE II*

PERIOD OF TIME COLOSTOMY OR CECOSTOMY WAS PRESENT BEFORE DETECTION OF CARCINOMA (9 CASES)	AGE, COLOR, AND SEX	TYPE OF ANORECTAL CARCINOMA	REFERENCE
Colostomy, 10 mo.	45, W, M	Squamous-cell carcinoma	Case Report 8†
Colostomy, 1 yr.	35, N, F	Adenocarcinoma	Ref. 2
Colostomy, 2 yr.	29, W, F	Squamous-cell carcinoma	Ref. 4
Colostomy, 3 yr.	Not stated	Squamous-cell carcinoma	Ref. 16
Colostomy, 7 yr.	Not stated	Squamous-cell carcinoma	Ref. 16
Colostomy, 8 yr.	49, N, F	Squamous-cell carcinoma	Ref. 12
Cecostomy, 12 yr.	32, W, F	Squamous-cell carcinoma	Ref. 4
Colostomy, 13 yr.	46, W, F	Adenocarcinoma	Case Report 1†
Colostomy, 18 yr.	Not stated	Adenocarcinoma	Ref. 20
		TYPE OF CARCINOMA OF CERVIX (2 CASES)	
Colostomy, 1 yr.	45, N, F	Squamous-cell carcinoma	Case Report 9†
Colostomy, 4 yr.	30, W, F	Squamous-cell carcinoma	Case Report 10†

*Eleven cases collected from the literature and the present series.
†Present series.

In those patients without severe scarring or extensive fistulous formation, conservative therapy utilizing rectal dilatations, chemotherapy, and supportive measures should be employed. As advocated by David in 1944,[30] a colostomy in conjunction with these conservative measures has in some cases afforded so much improvement as to warrant reanastomosis with apparent cure. It is important, however, to be aware of the persistent hazard of carcinomatous degeneration when such a conservative therapy is utilized. These patients must, therefore, be kept under close observation and, if it is feasible, biopsies must be performed at frequent intervals. In many instances a severely strictured rectum will prevent adequate biopsy examination.

As previously mentioned, the positive Frei test reverted to negative at the time of cancer detection in five cases; two of these were from my series. Further investigation should be made into this possibly anergic phenomenon in which a positive Frei test may revert to negative in the presence of carcinoma, since it is conceivable that such a skin test or a decrease in the complement fixation titer might serve as a diagnostic aid in the detection of latent cancer in these patients.

In my series of cases from Cook County Hospital, there was 4.5 per cent incidence of carcinomatous degeneration in patients whose conditions were

previously diagnosed as lymphogranuloma inguinale between the years 1937 and 1950. It is my opinion that had Frei tests and biopsies for carcinoma been performed on all of these 220 patients, a higher incidence of neoplasia might well have been observed.

Binkley and Derrick,[18] in 1945, reported the interesting observation that the average age in their series was lower in those cases of carcinoma of the anus with a positive Frei test, as contrasted with those with negative Frei tests. This observation is verified by my data in which twenty-eight of a total of thirty patients with anorectal neoplasms complicating lymphogranuloma inguinale developed carcinoma prior to 52 years of age, while the average age of onset of anorectal carcinoma in the general population is 54 years.[31] Swink,[24] in 1949, stated that although carcinoma in general is less prominent in Negroes, the incidence of neoplasms of the rectum and anus is considerably less in white than in Negro women at ages under 65 years. In 1951 Pund and Lacy[27] reported that in a group of forty-nine Negro patients with penile, vulvar, or anorectal carcinoma, 63 per cent had a positive Frei test. The incidence of carcinoma of the anus has been reported to comprise 1.7 per cent of anorectal cancer.[32] When the frequency of a positive Frei test in cases of squamous-cell carcinoma in the anorectal, vulvar, and penile areas is considered, these observations are all highly suggestive that lymphogranuloma inguinale predisposes to neoplastic degeneration.

The data collected from the literature and from my series of cases are not extensive enough to prove conclusively that lymphogranuloma inguinale per se predisposes to neoplasia. Rosser[33] maintained that the prolonged chronic inflammation with the fistulous formation present in these patients with lymphogranuloma inguinale is the factor responsible for the carcinomatous degeneration. The incidence of neoplastic degeneration reported in association with fistulas in ano is less than 1 per cent.[4] If my observation is correct, that a minimum of 4.5 per cent of patients with lymphogranuloma inguinale develop superimposed carcinoma over a period of years, then the predisposition of the chronic lymphogranulomatous inflammatory process to carcinomatous degeneration would seem apparent.

SUMMARY

1. In this series of eleven cases there was an apparent association between lymphogranuloma inguinale and carcinomatous degeneration.

2. The incidence of neoplasia in a group of 220 cases of lymphogranuloma inguinale, collected from the records at Cook County Hospital, was found to be 4.5 per cent.

3. In a survey of the literature, ninety-five cases were found in which lymphogranuloma inguinale and carcinoma were associated.

4. A colostomy does not remove the hazard of anorectal neoplastic degeneration in patients with lymphogranuloma inguinale.

5. Patients with less extensive anorectal disease may be treated with more conservative measures but must be followed closely. If the inflammatory process

continues after proper drug therapy and a preliminary colostomy, then more radical surgery is indicated.

6. Five cases are mentioned in which a previously positive Frei test reverted to negative at the time carcinoma was discovered. Further investigation is urged, as it is conceivable that this observation might form the basis of a diagnostic aid in the detection of latent carcinoma in these patients.

7. Evidence is presented from the literature and from my series supporting the hypothesis that lymphogranuloma inguinale may predispose to neoplastic degeneration.

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CARCINOMA OF THE MAXILLARY ANTRUM

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(From the Roswell Park Memorial Institute)

THE following is a brief survey of the records of the Roswell Park Memorial Institute, covering epithelial malignancies of primary origin arising in the maxillary antrum in contradistinction to tumors of similar histology occurring in the mucosa of adjacent structures, such as the alveolus, palate, nares, adjoining paranasal sinuses, and/or metastatic tumors secondarily spreading or extending into the antrum. A more recent ten-year period from 1936 through 1946 was chosen so that an over-all evaluation of five-year end results could be ascertained. All cases, even those too far advanced for treatment, are included.

In this particular period, sixty-eight cases of cancer of the antrum, or .14 per cent of all admissions, were noted out of 48,613 patients examined in this clinic where, over the past years, experience has shown that approximately 50 per cent of all patients seen are found to have some form of malignancy. This is an approximate incident of .27 per cent of all cancer, thus being higher than that reported by Perzik,[7] who found that carcinoma of the nasal cavity and paranasal sinuses makes up .2 per cent of all malignancies and 80 per cent of those cases in the antrum.

Of the 68 patients, 67.7 per cent were men and 32.3 per cent were women. Schall,[8] reporting a series of 219 cases of nasal cavity and sinus malignancies seen from 1930 to 1945, found 63 per cent in men and 36 per cent in women, which does not materially differ from our figures of exclusive epithelial malignancy of the antrum. To recapitulate, other types of antral involvement, such as lymphosarcoma, fibrosarcoma, giant-cell tumor, neurinoma, adamantinoma, and so forth, are not included in this study.

All of our patients were of the white or Caucasian race, except 2 who were Negroes. No particular nationality seemed to predominate. In this short series, the greatest incidence was noted in the 56-to-75-year age group, where approximately 58.8 per cent of our cases occurred (Table I). All, incidentally, had a negative serology.

Concerning etiology in this series, little positive information was gained, beyond that known of cancer in general. It is probable, however, as often postulated, that chronic inflammatory hyperplasia, with its tendency to polypoid formation and metaplasia of the mucosa, may play a part. The Cohnheim theory of occurrence in misplaced islands of embryonal squamous cells is also still suggestive.

Primary antral involvement is often difficult to prove as the lesion may have originated in the nose, ethmoid, hard palate, or alveolar mucosa, and

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secondarily involved the antrum. More essential from the prognostic point of view is an attempt to ascertain whether the process involves mainly the anterolateral wall and floor, or the posterior wall and roof of the antrum. In this respect, our experience coincides with that generally cited in that the former group, that is, the one involving the anterolateral wall and floor, offers a much better prognosis.

TABLE I. CARCINOMA OF THE ANTRUM (1936 THROUGH 1945, SIXTY-EIGHT CASES): TABULATION OF AGE, SEX,* AND PRESENCE OF METASTATIC NODES

AGE	NO NODES			NODES PRESENT			TOTAL	PER CENT
	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL		
35-45	9	1	10	1	1	2	12	17.6
46-55	5	3	8	2	1	3	11	16.1
56-65	13	5	18	4	2	6	24	35.3
66-75	5	5	10	4	2	6	16	23.5
76-85	3	2	5	0	0	0	5	7.3
Totals	35	16	51	11	6	17	68	100.0
Per cent	76.0	72.7	75	24.0	27.3	25	100	

*In the entire group, 67.7 per cent were men, 32.3 per cent were women.

Regional node metastasis, considered a sign of advanced disease, was noted in 25 per cent of our cases on initial examination. Perzik[7] stated that "distant metastasis occurs in over 25 per cent of cases of cancer in the nasal cavity and para-nasal sinus." Watson[12] found metastasis in 29 per cent of 127 cases, and considered lateral pharyngeal node involvement to run high.

Extension of the lesion to the orbit, nose, oral cavity, ethmoids, and cheek muscles is also to be considered as a significant indication of advanced disease, hence offering poor prognosis.

These observations, in addition to x-ray findings of bone destruction, led us to classify fifty-two of our sixty-eight cases in the advanced stage and sixteen in the earlier stages of the disease. These findings will be elaborated later when our results are considered. Age of the patient seemed to bear no essential relationship to prognosis in this series.

On histopathologic examination of the biopsied or autopsied tissues, thirty-eight of our specimens were of the differentiated types of squamous-cell carcinoma, either of the mucous membrane or pearl-cell variety, twenty-five were noted as anaplastic carcinoma, three as papillary, one as glandular epithelial formation, and one as epithelial neoplasm, possibly suggestive of adamantinoma. In twenty-seven cases the lesion occurred in the right antrum and in forty-one it occurred in the left. We believe that this is coincidental because of the small size of our series of cases.

The symptoms encountered were generally those commonly stated, such as swelling and aching of the cheek or teeth, nasal obstruction or bleeding, proptosis of the eye, all on the side of the lesion. In more advanced cases with extension through the infraorbital plate, the eye may be pushed up or proptosed with resulting diplopia, or involvement of the second division of the fifth cranial nerve may be noted causing numbness of the ipsilateral cheek and gums.

On palpation of the oral cavity, a resiliency of the anterolateral wall of the antrum, palate, or alveolus may be noted and is often a diagnostic sign. Extension into the orbit and roughening or destruction of the infraorbital ridge may be felt. The ipsilateral nares may be obstructed by displacement of the naso-antral wall or by extension of the tumor causing bleeding on attempted examination.

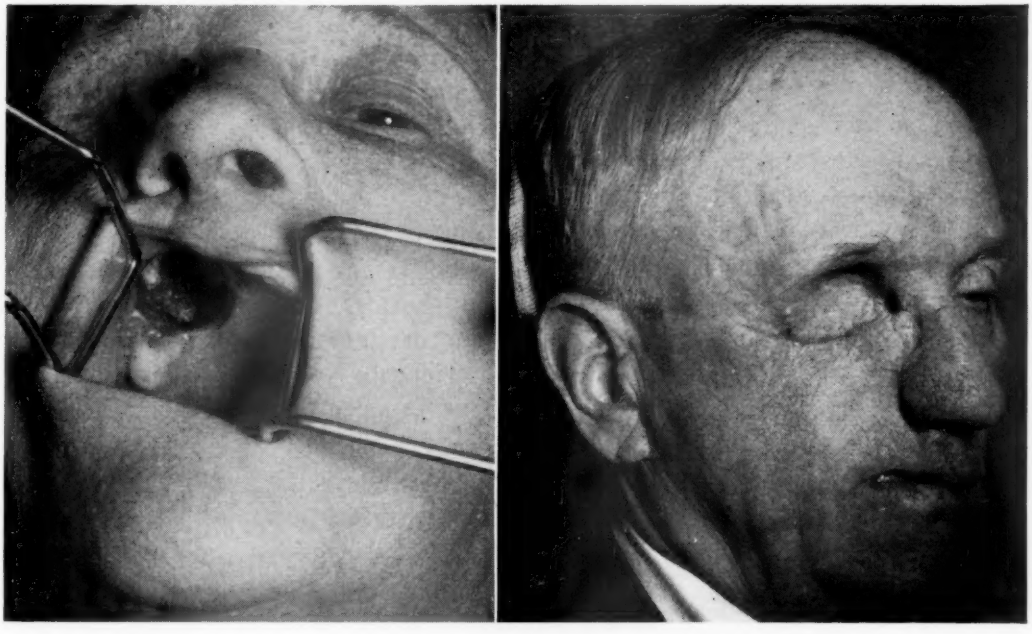
X-ray pictures of the chin-nose and lateral projection showed clouding of the antrum in sixty of our cases (88 per cent) and, incidentally, in all seven of our five-year survivals; sclerosis and/or marginal irregularity of outline was noted in twenty-five cases, or 36.8 per cent, and in 4 of the 7 patients surviving five years or more. Bone destruction was noted in twenty-three instances, or 33.8 per cent, but in only 2 patients surviving two years, 1 patient surviving three years, 1 patient surviving four years, and none surviving over five years. Usually, such patients lived less than one to one and one-half years. Thus, we must conclude that this finding is generally of bad prognostic import.

Fig. 1.—A typical seven-year arrest in a case of antral cancer following surgical drainage of antrum and irradiation.

Therapy during these ten years of investigation varied from external x-ray or radium pack to intra-antral radium tube, often supplemented with drainage through the naso-antral window, or modified Caldwell-Luc approach. The intracavitary radium tube was generally placed in the antrum and/or nose for 200 to 400 mg. hr. (100 mg. tube, 1 mm. of platinum for four hours) usually before x-ray therapy. X-ray therapy commonly consisted of one or more fields crossing in the antrum on 200 to 400 kv. modality with dosage up to tissue tolerance (Fig. 1). In a few of the cases, the palate was removed, the antral tumor tissue curetted out, and a radium mold applied with dosage to tissue tolerance supplemented by x-ray.

In more recent cases not included in this series, we have attempted to follow the principle of more radical surgery, that is, superior maxillary resection with or without exenteration of orbit and ethmoids where necessary, or a modified excision with electrocoagulation followed by intracavitary radium buried in gauge for dosages of 1,000 to 1,500 mg. her. (Fig. 2, *A* and *B*). This is followed later by external x-ray. This sequence of surgical drainage, radium, and x-ray in the present series of sixty-eight cases was often reversed as reflected in the results herein reported. We now believe that radical surgery and/or electrocoagulation followed by heavy dosage of gamma radiation up to 1,500 or more mg. hr. and these followed by x-ray to be the procedure of present choice, as is well shown by the results of Schall,[8] and as advocated by Weaver,[13] Schuknecht,[9] New,[6] Ward and Hendrick,[11] and others.

Results.—We divided the sixty-eight cases into sixteen early ones and fifty-three advanced cases as seen on admission and, as noted previously, we found that 7 of 16 patients with early cases survived from three to thirteen years (40 per cent). Six of these have been free of disease (Fig. 1) from seven to thirteen years (35 per cent arrests); 9 survived from two and one-half to thirteen years.



A. *B.*

Fig. 2, *A* and *B*.—Final results three months after exenteration of orbit and maxillary resection for antral cancer with invasion of orbit and skin of infraorbital cheek region.

Only 5 of 53 patients with advanced cases survived over two years under treatment of any kind. The longest survivals of patients with demonstrable bone destruction were three years, ten months and three years, three months, respectively. The average survival of such patients was seven months. The absolute survival rate of the 68 patients was 10.3 per cent in this series.

When the ten-year period from 1936 to 1946 is broken down into two five-year periods we note that the absolute five-year survival rate for the 1936-through-1940 period is approximately 6 per cent and that of the 1941-through-1945 period is 15 per cent. This is probably the result of more adequate surgical exposure and drainage in addition to the radiation in the later five-year period.

In the three-year period from 1943 to 1945 there were 18 patients with 7 living over five years, in fact, seven years or more, which constitutes 16.7 per cent of all patients as calculated on an absolute survival basis (Table II).

TABLE II. CARCINOMA OF THE ANTRUM (1936 THROUGH 1945, SIXTY-EIGHT CASES): TABULATION OF CASES BY YEARS

YEAR	DEAD	NOW ALIVE	TOTAL
1936	7	0	7
1937	8	0	8
1938	5	1	6
1939	7	1	8
1940	5	0	5
1941	6	1	7
1942	8	1	9
1943	6	1	7
1944	4	2	6
1945	5	0	5
Totals	61	7	68

Discussion.—Considerable literature has accumulated on cancer of the paranasal sinus and a lesser amount concerning the specific entity of cancer of the antrum. This is quite conceivable due to the difficulty in many cases, when the patient is first seen, of determining the site of primary origin.

Also, there has been considerable change in the methods of management from the earlier periods when radiation therapy was the mainstay, then through the period of less radical surgical procedures, such as electrocoagulation and drainage supplemented by irradiation, up to the present epoch when radical surgery with or without supplemental electrocoagulation and radiation is being advocated.

As the material presented here is concerned mainly with the first and second of these periods, we feel that the results herein stated may serve in a way as average end results achieved in a small series under such management.

Our 35 per cent five-year arrests in the earlier cases and 15 per cent absolute results in all cases for five years seem to be a fair average and fairly consistent with those quoted from other sources. For example, Holt Radium Institute[4] in Manchester, in a series of seventy-five cases, reported five-year survivals in 41 per cent of early cases, 14 per cent in more advanced cases, and a 25 per cent over-all survival rate.

Todd[10] in 100 cases and Windeyer[14] of Middlesex Hospital reported end results for five years as 26 and 25 per cent, respectively. Del Regato,[3] in a series of 10 patients treated exclusively by x-ray, noted a five-year salvage rate of 40 per cent and Lenz at Presbyterian Hospital noted 11 per cent.

Berven,[1] also using x-ray, achieved only 6 per cent five-year end results in 220 patients. It seems thus quite apparent that a greater number of cases under similar types of therapy must be collected before a stable base line of results by the various methods can be evaluated.

Schall[8] made a very substantial contribution to methods of management of these lesions when he showed in a good-sized series of 219 cases a 27 per cent five-year survival rate when surgery supplemented by radiation was used, 17.6 per cent when this sequence was reversed, and no lasting results from radium alone. Berven[2] at Radiumhemmet reported 38.4 per cent five-year survivals in 112 cases from electrocoagulation alone; New with 30 five-year survivals of 75 patients also reported a 40 per cent rate from electrocoagulation followed by radium and/or x-ray.

The future trend in therapy of these tumors seems, therefore, quite obvious, that is, radical surgery and/or electrocoagulation supplemented by irradiation (Fig. 2). Our later impression here would seem to bear out this conclusion.

SUMMARY

1. Sixty-eight cases of cancer of the antrum from 1935 to 1946 comprised .27 per cent of all cancer seen at the Roswell Park Memorial Institute. The prevalence in men was about twice that in women, with the greatest incidence between the fifty-sixth and seventy-fifth years.

2. The usual histopathology was squamous-cell carcinoma with a scattering of papillary carcinoma and adenocarcinoma.

3. The diagnosis was commonly made on symptomatology, physical findings, x-ray picture, and biopsy.

4. X-ray findings of cloudiness in the involved antrum were commonly noted. The finding of bone destruction carried a bad prognosis, as did also involvement of the orbital plate and posterior wall.

5. Treatment in this series was mainly by radiation often combined with conservative surgery, that is, surgical drainage, radium installation, and x-ray, with an absolute over-all five-year cure rate of 15 per cent in all cases and a relative rate of 35 per cent in early cases.

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LONG-ACTING DRUGS FOR AVOIDANCE OF POSTHEMORRHOIDECTOMY PAIN: A NEGATIVE REPORT

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RECENTLY a repository injection of d-tubocurarine chloride[1] and a "new" anesthetic solution[2, 3] have been advocated for the control of pain following hemorrhoidectomy,[1-3] as well as pain following other anorectal operations.[3] I have received a large number of inquiries concerning the merits of these agents, particularly the anesthetic solution, from general surgeons, anesthesiologists, gynecologists, and general practitioners. It is, therefore, timely to report the results of the following study concerning the pain-relieving features of these agents, especially since the virtues of prolonged local anesthesia have even been communicated to the layman, who is demanding it (Galton, L.: Cosmopolitan, May, 1953, p. 22).

MATERIALS AND METHODS

One cubic centimeter of a suspension containing 25 mg. of d-tubocurarine chloride pentahydrate and chlorobutanol 0.5 per cent in a menstruum of peanut oil, oxycholesterol derivatives, and 2 per cent of beeswax, marketed as Tubadil, was injected into one of the deltoid muscles prior to the commencement of hemorrhoidectomy in 11 alternate patients. Another eleven alternate hemorrhoidectomies served as controls. All patients were operated upon under regional, saddle-block spinal, or caudal anesthesia.

A solution containing 1 per cent procaine, 0.25 per cent procaine hydrochloride, and 5 per cent butyl p-aminobenzoate in a solvent composed of 2 per cent polyethylene glycol-300, 78 per cent propylene glycol, and water, marketed as Efocaine, was injected into the perianal tissues in a dosage varying from 5 to 10 c.c., by the methods employed either by Tucker[2] or Gross,[3] at the conclusion of thirty-nine alternate open-type hemorrhoidectomies.[4] Another thirty-nine alternate open techniques of hemorrhoidectomy served as immediate controls; these in turn were fortified by a recent study of 535 personally performed hemorrhoidectomies.[4] Low or saddle-block spinal or caudal anesthesia was employed.

The nurses, who knew nothing about this clinical experiment, had been instructed to give the patients pain-relieving drugs such as morphine or Demerol by injection on the complaint of pain only (morphine was more desirable than Demerol). In addition, orders for the oral administration of hypnotic drugs and/or pain-relieving coal-tar derivatives were left to be used at the discretion of the nurses in attendance, particularly for sedation against apprehension and restlessness.

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About eight hours after the operation, when the effects of spinal anesthesia were dissipated, most of the patients were made ambulatory. During that eight-hour period the patients received abundant amounts of fluid given primarily as an aid for the prevention of postspinal headache. Those patients who could not void while in the lying position were permitted to stand out of bed whenever they developed the urge to urinate. The day following the operation, all patients were given regular house diets, and hot hip baths were begun. Those patients who had been operated upon under caudal anesthesia were served food immediately after operation, and most of them were ambulatory almost from the outset.

Originally it was planned to extend these studies to at least 100 cases in each series. However, as this investigation progressed and the results revealed themselves, I could not justify the continuation of this clinical experiment.

RESULTS

Seven of the 11 patients who had received the d-tubocurarine required one to two doses of either morphine or Demerol for the relief of pain. Two of the 4 patients who did not require narcotics exhibited some general muscular relaxation but without respiratory embarrassment. Another patient (the eleventh of this series) could not talk for almost ten hours, appeared flaccid, and had sufficient difficulty in breathing so as to alert the anesthesiologist for fear that artificial respiration might become necessary.

Of the controls, 3 patients did not require narcotic drugs for the relief of postoperative pain.

Postoperative pain requiring one to two doses of morphine or Demerol was complained of by 27 patients following the injection of the anesthetic solution; 2 additional patients required three doses of narcotics because of a combination of pain and a peculiar burning sensation, the latter lasting in various degrees of intensity for more than five days. Thus, 29 patients had postoperative pain requiring an analgesic narcotic drug for its control. Burning sensation was complained of by 2 patients without direct questioning and by 5 more patients who registered this complaint on direct interrogation. Pain during the first act of defecation was mild in 8 patients and only moderate, although erratic, in severity in the remaining patients. Edema, hyperemia, and occasional bleeding were noted in the wounds of nine patients; the burning sensation already alluded to was present in 4 of these 9 patients. Some delay in the healing of the anorectal wounds was present in 7 of these 9 patients and in 3 other patients of this series. The wounds of 4 patients had failed to heal completely until the end of the fifth postoperative week, and did not heal until the end of seven weeks in 6 other patients. However, once healed the wounds remained well healed and were indistinguishable from those of the controls. Garson[5] independently has obtained somewhat similar results in fifty-four anorectal operations, including many hemorrhoidectomies.

Fecal incontinence lasting for from sixteen to thirty days was observed in 3 patients, all of whom exhibited the peculiar burning sensation and delay

in the healing of the wounds. In two instances, the patients had some warning so that they could "hurry" to the lavatory, while the third patient had to be confined to her house for about one month.

Twelve of the control patients required no morphine; 23 had received one to two injections, and 4 patients were given three injections of narcotic drugs. All patients had experienced somewhat more pain during the postoperative first act of defecation; this pain was, however, always relieved promptly by a hot hip bath and has never constituted a problem in either the control or the injected cases. None of the other complications was noted in the controls.

Additional Data.—To this absolutely personal experience may be added the occurrence of a localized suppuration in a patient on one of my services several days posthemorrhoidectomy, which was performed by a competent associate (Garson) who has had a much wider experience with the use of this drug than I have had. Similar experiences have been reported to me by other surgeons.[5] I have also seen similar suppurations and/or areas of necrosis following the injection of this anesthetic solution for the "conservative" treatment of anal fissures.* Squire and Weiner,[5] as well as other obstetricians, have observed necrosis in episiotomy wounds. Intractable paresthesias, similar in character to those observed following injections of procaine hydrochloride or its derivatives,[6] occurred in 2 patients approximately three weeks after this solution was injected deeply subcutaneously for the control of anal pruritus. As in the case of other long-acting "anesthetics," complications following Efocaine such as "postinjectional suppurations are unreported for various obvious reasons."[6]

DISCUSSION

Using personal experience and a recent comparative study of the open versus the closed methods of hemorrhoidectomy[4] as a background for this investigation, I believe that pain following hemorrhoidectomy has to a large degree a direct relationship to the type of technique employed. It was shown that following the open technique, which consisted of a sharp dissection of the hemorrhoidal mass well beyond the mucocutaneous or dentate line without suturing of the wound except for the mucosal pedicle (which in principle is a Milligan-Morgan procedure), the patient seldom required more than two doses (usually 0.01 Gm. or ⅙ gr.) of morphine postoperatively for relief of pain; narcotic drugs were unnecessary for the control of restlessness or apprehension. Significantly, about 40 per cent of these patients required no morphine at all; coal-tar derivatives and/or barbiturates sufficed for sedation in these patients. However, following a semiclosed method of hemorrhoidectomy, which was essentially the same as the open type except that the subcutaneous structures of the hemorrhoidal bed were approximated but without suturing of the skin, all patients required morphine for postoperative sedation, and more than two doses had to be used in a considerable number of these patients. Importantly, following the closed type of hemorrhoidectomy in

*M. H. Adelman, an anesthesiologist who has participated in parts of this work, has encountered two instances of chronic, slowly healing ulcers on the chest wall following the injection of this solution into the "trigger zones" for relief of pain.

which the wounds, including the skin, are closed by suture following the excision of the hemorrhoidal mass, about four times more morphine was required for the control of postoperative pain than after the open operation.

The competence and gentleness of the surgeon also enter into this picture. In 1941, referring to the pitfalls and hazards of the then heralded slowly absorbable, oil- or water-soluble anesthetic agents which have since fallen into considerable disrepute, I stated that "numerous competent proctologists have questioned the wisdom and need for the employment of the anesthetic agents when clean-cut and gentle surgery and meticulous preoperative and postoperative care are utilized. Following a well-performed surgical anorectal procedure there should be no need for these anesthetic agents; at best these drugs are poor substitutes for good surgery. I have never found a need for the employment of these drugs for the avoidance of postoperative pain"[7]; this still holds true.

Gross,[3] in a study of sixty-five cases including some forty-five hemorrhoidectomies, stated that "35 patients required no postoperative medication, 28 received one or two doses, and 2 patients received three doses of postoperative medication." He, however, summarized his studies thus: "Efficient pain control was achieved in 96 per cent of anorectal surgery series in which patients required one or two doses of postoperative medication." Tucker[2] reported that 32 (80 per cent) of his 40 patients had received no doses or one dose of postoperative medication, while 4 (10 per cent) had received two doses and another 4 patients (10 per cent) had been given more than two (varying between four and six) doses. To me "efficient pain control" means no pain and, consequently, no need for any drugs, neither of which was accomplished in all cases by Gross or Tucker, who are the present proponents of injectional proctologic postoperative anesthesia. Their figures, therefore, do not seem to entitle this drug to the designation of anesthetic, as absolute postoperative anesthesia had not been produced.

The lesson I have learned is clear: considering that about one-third of patients who undergo the open type of hemorrhoidectomy do not ordinarily require morphine for postoperative sedation[4] and that the pain in the remainder of the patients can be easily controlled on the average by two doses of morphine, I find little, if any, need or justification for taking even the slightest risk by injecting any of the slow-absorbing "anesthetic" agents. Garson[5] has also indicated a dissatisfaction with such drugs. This also applies with equal force to repository injections of d-tubocurarine, as I was not impressed with the alleged "abolition of painful spasm of the sphincters—practically the only source of pain following hemorrhoidectomy."[1]

Parenthetically, if it is desired, pain following a properly executed open type of hemorrhoidectomy can be safely and effectively prevented by the employment of the simple classic or modified sphincterotomy as described for the treatment of chronic anal fissure.[8] I employ this maneuver at the conclusion of hemorrhoidectomy only when preoperative spasm of the anal sphincter mus-

cles of undetermined origin accompanies hemorrhoids. However, there seems to be little or no justification for the routine employment of sphincterotomy following hemorrhoidectomy.

Edema and hyperemia with some delay in the healing of the anorectal wounds were observed in ten patients although, once healed, the wounds were indistinguishable from those of the controls. In these cases, complete healing failed to take place within the usual three- to four-week interval observed in the control cases as well as in the hundreds of other patients operated upon by the identical technique.[4, 6] It is possible that these phenomena may be caused by the adverse, although temporary, degenerative effect exerted by the injected anesthetic solution on the innervation of the anorectum. Experimentally, using guinea pigs, rats, and rabbits, Weinberg[9] has noted a fibroelastic proliferation about injected nerves during the early postinjectional stages which, however, disappeared in time; concerning this he stated that "one is dealing with a benign process which is apparently reversible." He has also observed macroscopic "necrosis in the line of injections" of the muscles as well as microscopic "necrosis and partial disappearance of muscle fibers with a replacement by a moderately cellular, loose connective tissue" with "little or no inflammatory reaction" in those experimental animals that had been submitted to autopsy up to thirteen days after the injection of the anesthetic solution. Neither "a foreign body giant cell reaction" nor "significant permanent damage" was observed, except in one instance in which a "small focal area of fibrous replacement of muscle fibers" was noted at necropsy performed some time between eighty-nine and ninety-eight days following the injection of the solution. The clinical and histopathologic aspects of this problem need much more urgent investigation, particularly as they apply to the tissues of the human anorectum, one of the most potentially, if not actually, grossly infected areas in the body.

Fecal incontinence, although temporary, carries an undesirable psychologic import and is quite annoying.

SUMMARY AND CONCLUSIONS

1. Repository injection of d-tubocurarine does not appear to control posthemorrhoidectomy pain. The generalized muscular relaxation observed in three cases, which was alarmingly pronounced in one patient, constitutes a potential respiratory danger.

2. The failure of an anesthetic solution, injected into the perianal tissues at the conclusion of thirty-nine hemorrhoidectomies, to eliminate postoperative pain completely in a significant number of cases (which is also reported by the proponents of postoperative injectional anesthesia) plus the occurrence of complications such as temporary fecal incontinence, frank suppuration, and/or necrosis, noted by others, lead me to believe that postoperative injectional anesthesia is not a procedure to be used.*

*Since submission of this paper for publication, the neurological complications[10] and even death[11] following the use of Efocaine have been reported. Efocaine is now regarded by some former users as an unsatisfactory medicament because of complications noted in late postoperative examinations.[12]

3. In my experience, severe pain after operation or during the first act of defecation does not follow a well-performed open type of hemorrhoidectomy. The pain observed following the open type of hemorrhoidectomy performed upon a non-neurotic person can be controlled safely and effectively with ease by sedatives or analgesic drugs. These drugs also effectively allay preoperative and postoperative apprehension and are given freely, as a matter of sound practical therapeutics, to all patients who have a natural fear of any operation.

ADDENDUM

Since submission of this paper for publication, Mannheimer, Pizzolato, and Adrian[13] have stated that, like alcohol and phenol, Efocaine and the vehicle in Efocaine "cause anesthesia by nerve destruction rather than by blockade due to their anesthetic effects."

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MECHANISM OF OMENTAL MIGRATION

A Review of the Literature and Experimental Study*

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INTRODUCTION

THE presence of the omentum at sites of inflammation throughout the abdominal cavity, with its attempts to wall off and protect against infection, has been recognized since ancient times. The mode of travel of the omentum from its normal position to the site of inflammation is not so definitely understood. If the most important function of the omentum is considered to be its ability to limit or wall off peritoneal insults by the formation of adhesions, it is necessary to assume that, in order to be efficient at its job, it must travel or migrate into contact with the offending agent or to the site of inflammation. It is the object of this work to attempt to explain the migration of the omentum.

Historically, there has been much speculation on the function and mode of travel of the omentum. Hippocrates (460 to 385 B.C.)[2] associated the omentum in some way with the formation and absorption of intraperitoneal fluid. Aristotle (384 to 322 B.C.)[3] regarded the omentum as a fatty apron designed to protect the intestines against cold. Vesalius (1514 to 1564)[3] thought of it as a fixation ligament or supportive ligament for the transverse colon. Ross[16] in 1893 assumed that the omentum protected the intestines against injury by assisting them in gliding away from the point of greatest pressure. He observed the way the omentum seemed to hasten to prevent the invasion of the general peritoneum by some intraperitoneal poison, gluing itself to the site of inflammation and thus preventing dangerous invasion of the general peritoneal cavity. "It is like a man-of-war ready to sail to any port in which there is impending trouble."[16]

Durham[8] in 1897 cited the omentum as the seat of selection for the cells being removed from the peritoneal fluid after bacterial contamination.

Buxton and Torrey (1906)[4] described the omentum as a battleground or area of support for phagocytosis by the macrophages and the polymorphonuclear leukocytes of inert particles and microorganisms in the peritoneal cavity.

Rutherford Morison (1906)[12] was the first to recognize the importance of the omentum in arresting the spread of inflammation by forming adhesions around its borders. Fisher[9] in 1906, Ruben[19] in 1911, Schutz[20] in 1930, and Rothenberg and Rosenblatt[18] in 1943 made similar observations regarding the

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part played by the omentum in intraperitoneal inflammation, namely, that the most important function of the omentum is the part that it plays in limiting intraperitoneal inflammation.

Other functions, such as neutralization of toxins,[6, 14] plugging of peritoneal openings to prevent herniation,[12] providing a blood supply to a tissue or organ not adequately nourished,[3] providing a vascular bed for the relief of arterial tension,[7] providing a direct avenue from the peritoneal cavity into the vascular system,[15] and causing leukogenesis,[21] have all been ascribed to the omentum.

Finding the omentum frequently at the site of inflammation, at the operating table and in the post-mortem room, has led surgeons and pathologists alike to speculate concerning the motion of the omentum. Many theories of motion have evolved.

Ross,[16] in 1893, wrote that the omentum was endowed with some vermicular-like action and that it was able to move itself from place to place. Durham (1897)[8] noted that the omenta of animals dead of peritoneal infection became rolled and folded up because of the peristalsis of the intestines. Adami (1898)[1] thought that the omentum was endowed with the power of active locomotion. He thought of it as rolling up and down to the right and left and in effect, covering the entire abdominal cavity. Morison (1906)[12] believed that the omentum was attracted to the point of injury by some sort of information. He likened its movement to that of a jellyfish.

Theodore Fisher (1906),[9] Norris (1908),[13] Wilkie (1911),[23] and Adams (1913)[2] believed that the movement of the omentum was dependent on peristalsis of the intestines. Fisher postulated that if the peristalsis affected all areas of the intestines, the omentum was spread out over the intestines; however, if there were paresis of one segment of the intestines, the active, moving segments propelled the omentum to the area of stasis.

Dickinson (1906)[7] postulated that the position of the omentum in the abdomen was determined by (1) pumping action of the diaphragm, (2) intra-abdominal pressure, and (3) peristaltic movement of the intestines.

Rubin (1911)[19] denied spontaneous motility of the omentum. Like Wilkie and Adams, he denied the theory of a positive or negative chemotaxis of the omentum as advocated by Milian.[19] His theory of motion was similar to that of Dickinson.[7]

Hertzler (1935)[11] stated that if there were no leukocytic-cell infiltration into the omentum, there would be no migration. He explained the motion as similar to the influence that draws any leukocyte to an area of infection or inflammation. He did not believe that the position of the normal omentum was influenced by a change in the position of the individual or animal, or that peristalsis influenced the advance of the omentum to the site of injury. "If we are to speak of the 'intelligence' of the omentum, we may safely add that an individual's omentum is as smart as his leukocytes."[11]

Schutz[20] in 1930 approached the mechanism controlling migration of the omentum from an entirely different point of view and one not previously presented. He likened the motion of stretching out of the omentum to the

uncoiling of a curled-up garden hose when an increased pressure of water is caused to flow through it. Similarly in the omentum, he postulated that the arteries become hyperemic, the intra-arterial blood supply is increased, the arteries straighten out, and the omentum loosely attached to the arteries is pulled by them to their advanced position. He noted a resemblance between the omentum and erectile tissue.

Cantacuzène and Soru (1931)[5] stated that the migration of the omentum to a lesion of the intestines was strictly a function of the difference of electric potential that existed between these two points. They determined that the electric potential between the omentum and the intestines was usually 8 or less millivolts. After an injury to the peritoneal surface, the electric potential between the two areas was immediately elevated to 53 millivolts. The omentum, which was electronegative under normal conditions, became electropositive; thus, the omentum was attracted to the injured area.

Rothenberg and Rosenblatt (1942)[17] by means of omental-marking agents and fluoroscopic studies concluded that omental migration depended on the motion of the underlying bowel.

Thomas, Greene, and Rhoads (1950)[22] studied the process of adhesion formation through abdominal windows made of methyl merhacrylate or Lucite in animal experiments. In the course of their observation they stated that, in respect to an area of injury, the omentum seems to be pushed or attracted to the sticky coagulum to which it adheres.

In summary, it is seen that, in the literature, omental migration has been attributed to (1) an inner intelligence, (2) peristalsis, (3) action of the diaphragm, (4) intra-abdominal pressure, (5) positive or negative chemotaxis, (6) leukocytic-cell infiltration, (7) arterial hyperemia, and (8) change in electric potential.

It is the object of this experimental work to study the mechanism of omental migration and thereby make steps toward an accurate, simple, and scientific explanation for the migration of the omentum.

Experimental Data.—An omental-marking agent for radiographic recording was selected. Studies were made of the normal omental pattern, omental pattern response to food and starvation, omental pattern response to peristalsis, omental pattern response to experimental appendicitis, omental pattern response to sterile gauze in right lower quadrant of abdomen, omental migration in response to inaccessible inflammation (1. sterile gauze sutured to undersurface of diaphragm and 2. experimental liver abscess), omental migration in response to increase in omental blood volume flow, dilation of the omental bed with maintenance of systemic pressure, and the omentum in an isolated fluid medium.

Dogs were used in all animal experiments. They were healthy adult mongrel dogs weighing five to fifty pounds, both male and female. All dogs were fed standard basic diet for laboratory dogs and were kept in cages throughout the experiments.

All operative procedures were performed on anesthetized dogs which were given veterinary Nembutal in the jugular vein in the amount of 1 gr.

for each five pounds of weight. Subsequent maintenance doses were given throughout the procedure as indicated, and all operations were performed using aseptic technique. All the dogs used in the experiment were studied for movement of the omentum uninfluenced by intraperitoneal procedures.

X-ray pictures were obtained on all dogs immediately after the operation while the dog was still anesthetized and at two subsequent intervals, making a total of three sets of films. Anteroposterior and left-lateral abdominal films, size twelve by fourteen inches, were obtained. A Bucky diaphragm was used with a time of one-fifth second and a distance of thirty-six inches. Three hundred milliamperes were routinely employed, and the kilovoltage depended on the size of the dog.

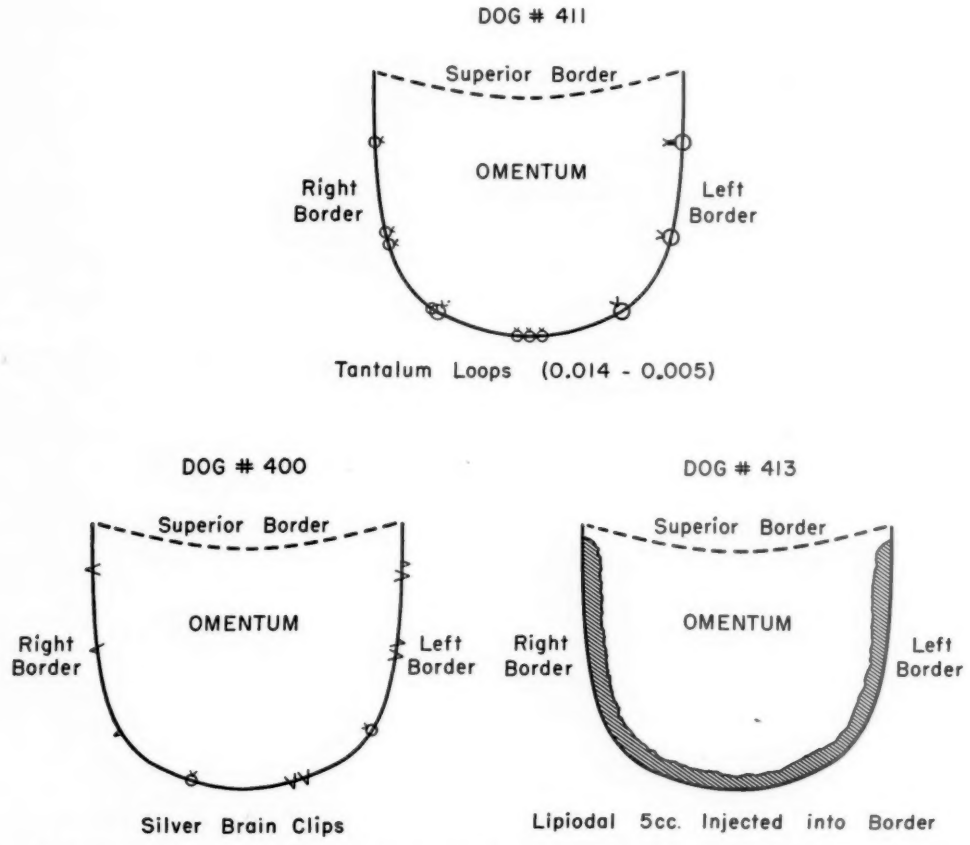

Fig. 1.—Diagram of omental-marking agents and their sequence in the omental edge.

Selection of a Marking Agent.—As a preliminary experiment it was necessary to determine an agent that would mark the omentum in such a fashion that its position could be determined roentgenographically. Four requirements had to be met in order for the agent to be used: (1) it had to be radiopaque; (2) it had to cause minimal tissue reaction; (3) it had to be light in weight, thus eliminating a static effect; and (4) it had to retain its position as originally placed in the omentum.

Three agents were chosen for testing: (1) tantalum wire loops (ethicon tantalum surgical wire sutures, Size 0.005 and 0.014), (2) silver brain clips, and (3) Lipiodol Lafay (E. Fougera and Company, Inc., New York, N. Y.).

In each experiment, the abdominal cavity of an anesthetized dog was entered through a short midline epigastric incision. The omentum was gently drawn out of the abdominal cavity and carefully inspected for adhesions. The omentum was kept moist with physiologic saline solution throughout the procedures. The marking agents were placed in the omental edge as atraumatically as possible, and the omentum was then returned to the abdominal cavity and the abdominal wound was closed in layers. Diagrams of the omentum containing the marking agents are seen in Fig. 1.

Results.—

Dog 411 (omentum marked with tantalum wire): In each film the tantalum loop could be identified as such; however, some of the loops were superimposed, and identification as to the actual site of the loop in the original sequence was often impossible. A second difficulty proved to be chance profile of an occasional loop on edge so that its character could not be identified. In an area of the loop, there was no evidence that the loop exerted a drag effect on the omentum and, in each instance, the loops had maintained their original position in the omentum.

Dog 400 (omentum marked with silver brain clips): The clips were very difficult to interpret. Although they were radiopaque, they were set at various angles, thereby making their identification in the sequence impossible without multiple oblique films. At time of operation, it was difficult to secure the clips in the omental borders, and at post-mortem one clip had been dislodged (possibly while returning the omentum into the abdominal cavity) from its original setting. As with tantalum loops no gross tissue reaction to the silver brain clips could be determined at autopsy.

Dog 413 (omentum marked with Lipiodol): X-ray pictures of this dog were obtained immediately following operation, twenty-four hours following operation, and fifteen days following operation. The first two sets of x-ray pictures showed an irregular opaque mass approximately 6 by 6 cm. in the anteroposterior view. Fifteen days following injection there was still faint evidence of the presence of the opaque oil in its original position; however, its outlines could not be determined, and the shadow it cast was not unlike that of fecal matter in the intestines. The Lipiodol gradually shifted away from the omental border toward the greater curvature of the stomach. Here again there was little gross evidence of tissue reaction in the Lipiodol.

Results: It was concluded that tantalum wire was by far the best marking agent of the three agents studied; therefore, it was used exclusively in subsequent experiments. Because of the complicated sequence originally used and the difficulty in the interpretation when loops became superimposed, it was decided to mark the right border of the omentum with three single tantalum loops appropriately placed and the left border with three double loops, one small and one large, similarly placed (Fig. 2).

Normal Omental Pattern.—Since it had been suggested that the omentum under normal circumstances traveled to different parts of the abdominal cavity,[7, 23] it was thought necessary to determine the position of the marked omentum under physiologic conditions at various time intervals. If the omentum routinely migrates to different parts of the abdominal cavity, this should be demonstrated by a change in the position of the tantalum loops and an over-all change in omental pattern. It was presumed that there were no omental adhesions after placing the loops, and this was proved in all instances at later operation.

Ten dogs with marked omenta which had been x-rayed immediately following operation were then x-rayed each week for a period of three weeks. In one of these animals, x-ray pictures were obtained at weekly intervals for eight weeks following operation. All dogs were maintained on ordinary laboratory diets and were allowed freedom of their cages for the entire period. Both anteroposterior and left lateral films were obtained. Although a complete outline of the omentum is not expected, a general picture of the change in omental pattern can be obtained from the displacement of various loops. At time of obtaining the x-ray pictures the dogs were not sedated; however, they were centered on a crossbar on the x-ray table in an effort to have each film taken from the same position as the previous one.

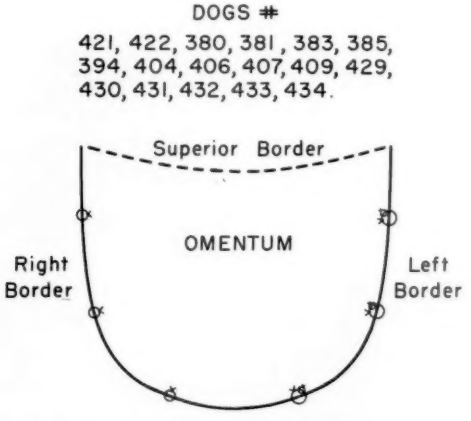

Fig. 2.—Diagram of omental outline with tantalum loops as marking agent. Pattern used in later experiments.

Results: A diagram of the omental pattern from one of the ten dogs presenting the apparent position of the omentum on successive weeks is shown in Fig. 3. The single loops represent the right border and the double loops represent the left border. The remaining nine dogs present similar patterns.

From the diagram it is seen that although the general pattern of the edge of the omentum changes considerably in most instances during ordinary unrestrained existence of the dog, the omentum, however much its border varies, lies in approximately the normal relationship to the upper abdominal organs and does not appear to fold on itself or migrate cephalad to its normal line of attachment.

Omental Pattern Response to Food and Starvation.—Since the omentum is so closely related both in position and blood supply to the stomach it was decided to study the effects of feeding and starvation on the motion of the omentum. Three marked dogs were used. (1) Dog 421 was starved for twelve hours prior to the first film and was allowed no food whatsoever for the duration of the experiment; (2) Dog 404 was starved for twelve hours prior to the first film

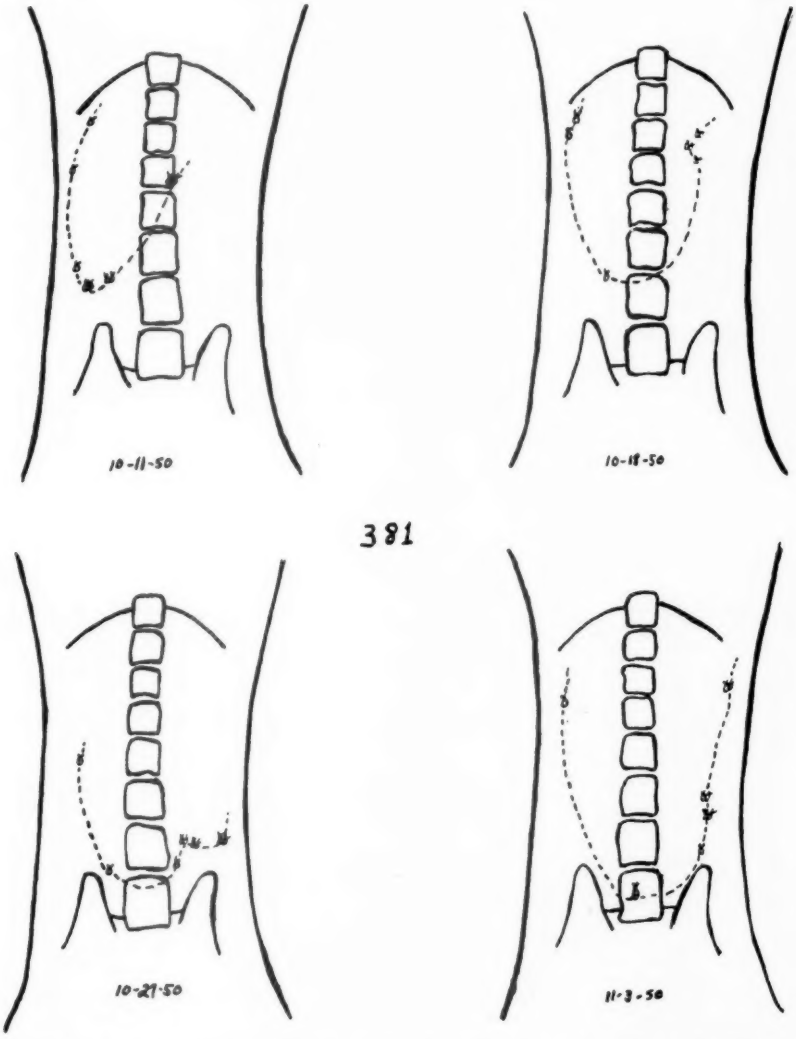

Fig. 3.—Normal omental pattern. Single loops in right omental edge; double loops in left omental edge. Seven-day, nine-day, and seven-day interval.

but was given food as desired for twenty minutes before each x-ray exposure. In the interim he was given no food; (3) Dog 409 was maintained on normal laboratory routine with no change in feeding habits, that is, with available food in the cage at all times.

Films were taken initially and at six, eighteen, and forty-two hours. The total period of starvation was fifty-four hours.

The diagram of each film is presented (Figs. 4 through 6).

Results: The most marked pattern change is seen in Dog 404 (dog given food as desired for twenty minutes before each film). Although this change is not marked, it is unmistakable and is thought to be explained by the increased peristalsis initiated by feeding.

The pattern of the starved dog and the control dog remain fairly constant and are not outside the range of ordinary movement as seen in the second experiment.

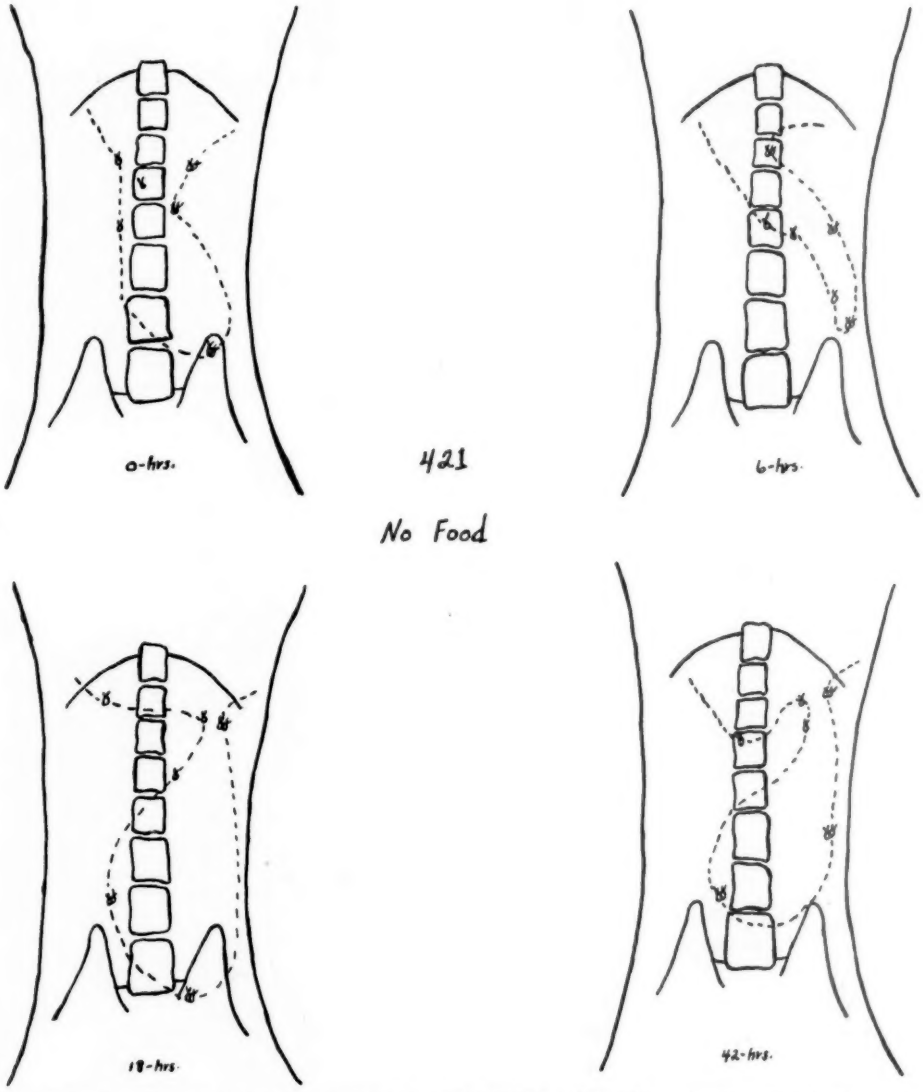

Fig. 4.—Omental pattern response to starvation (fifty-four hours' duration).

It is concluded that peristalsis plays a part in the motion of the dog's omentum.

Omental Pattern Response to Peristalsis.—In order to study more fully the effects of peristalsis on the motion of the omentum, Dog 409 was anesthetized

with intravenous veterinary Nembutal and tied to a frame, in the dorsal supine position. The dog had been allowed food for twenty-eight hours.

Dog 409: Twenty-five cubic centimeters of castor oil was given per os, and films were obtained at one-half hour, one and one-half hours, two and one-half hours, and three and one-half hours. During this time the anesthesia was

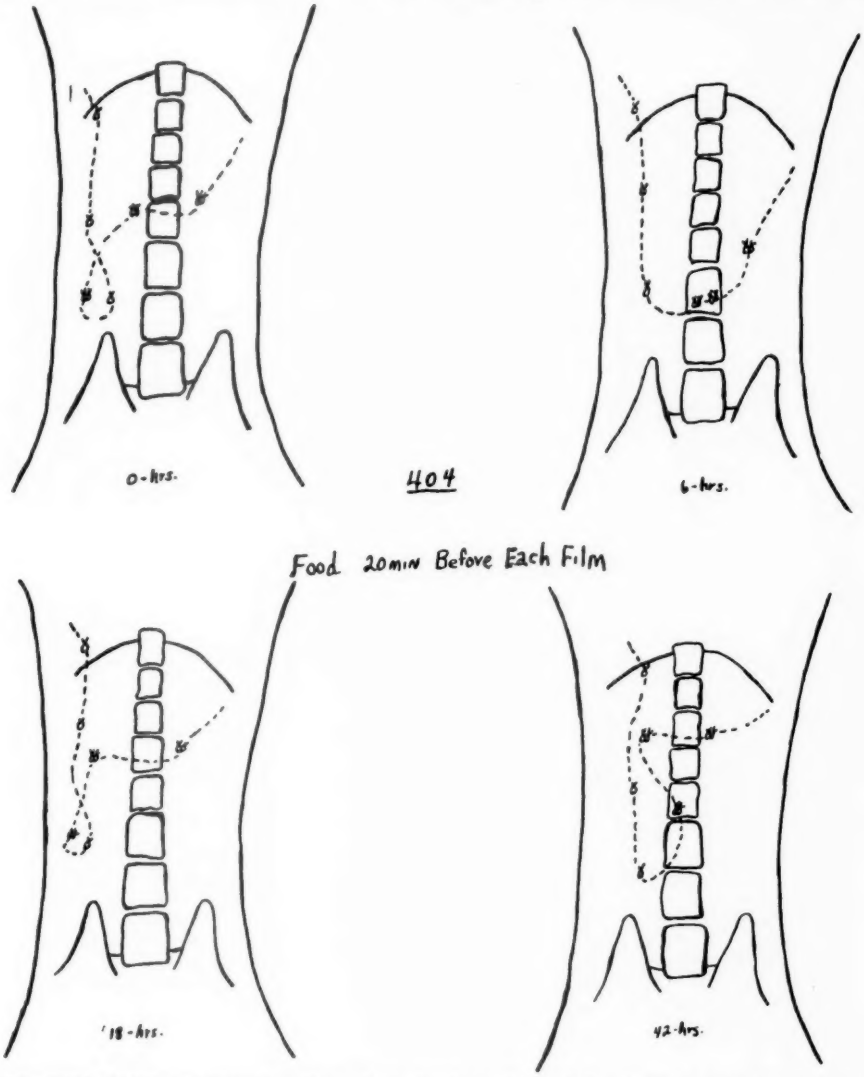

Fig. 5.—Omental pattern response. Dog given food as desired for twenty minutes prior to film, starved in interim.

continued and the dog was constantly observed. There was no visible peristalsis, and peristaltic sounds were heard with auscultation of the abdomen. The pattern of the dog's omentum during a period of three and one-half hours is diagramed (Fig. 7).

Since there was no visible or audible stimulation of peristalsis and since the pattern diagrams showed no appreciable motion of the omentum, the dog was then given 2 c.c. of 1:2,000 Prostigmine intravenously. Within five minutes,

marked waves of peristalsis could be seen through the abdominal wall. The dog defecated and passed flatus. Films were taken fifteen and thirty minutes after the injection; diagrams of the omental pattern are presented (Fig. 8).

Results: Castor oil fails to initiate peristalsis in the anesthetized dog over a period of three and one-half hours and fails to change the omental pattern. Prostigmine given intravenously is followed by marked peristalsis and a definite movement of the omental edge.

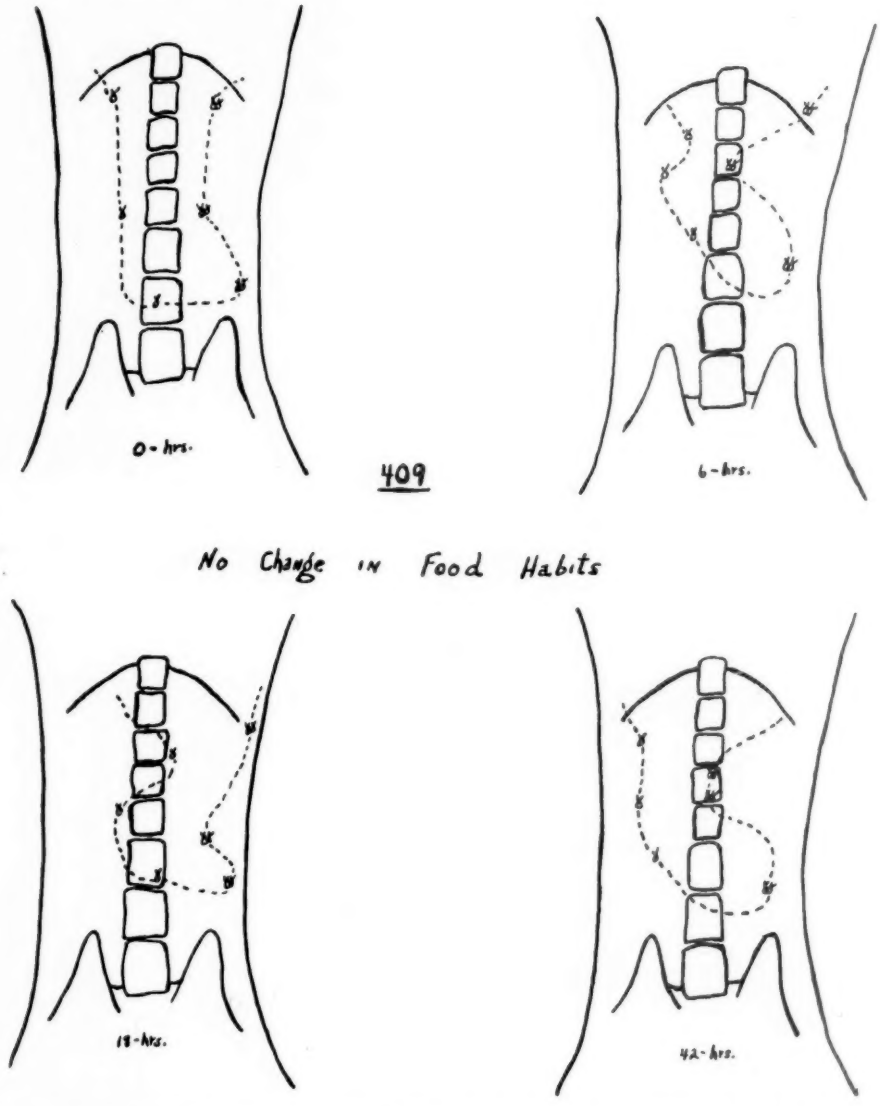

Fig. 6.—Omental pattern response. No change in food habits; control for this experiment.

It is concluded that peristalsis in the underlying intestines causes migration of the omental edge.

Omental Pattern Response to Change of Position.—Since there was shown to be considerable variation in the position of the omentum in day-to-day

observation it seemed of interest to determine whether gravity as well as peristalsis played a part in this movement.

A dog with a marked omentum was anesthetized and securely fastened in the dorsal supine position to a wooden frame, and a film was obtained. The dog was then placed in a vertical position with the head down for fifteen minutes and at the end of this time another film was obtained. Again

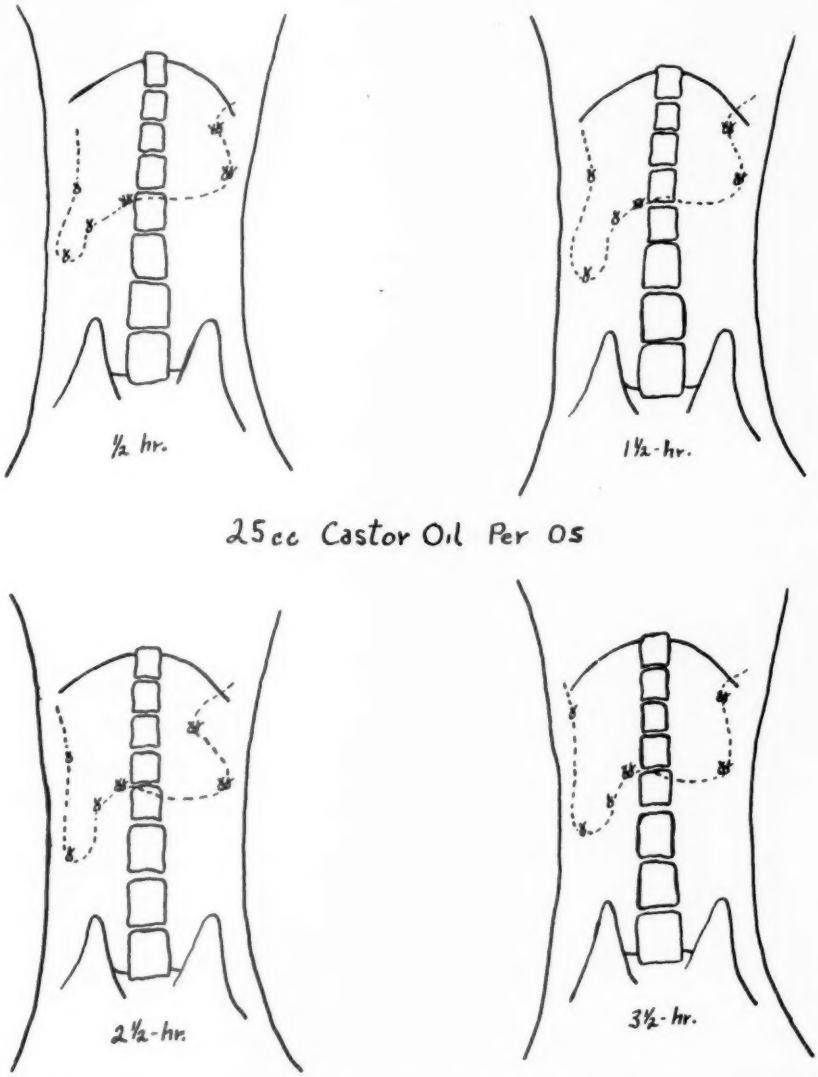

Fig. 7.—Omental pattern response to castor oil. (No visible or audible peristalsis produced by the castor oil.)

after being horizontal for fifteen minutes, the dog was placed in a vertical position for fifteen minutes with the head up, and a third film was obtained. Diagrams of the omental pattern are presented (Fig. 9).

Results: It is seen that there is a marked shift in the omental pattern corresponding to the change in position of the animal. The omentum seems to

move as a unit rather than to fold on itself. It is concluded that gravity is a factor in omental movement.

Omental Pattern Response to Experimental Appendicitis.—Five dogs (Nos. 433, 385, 383, 404, and 381) with marked omenta were used in a study of omental migration in response to experimental appendicitis.

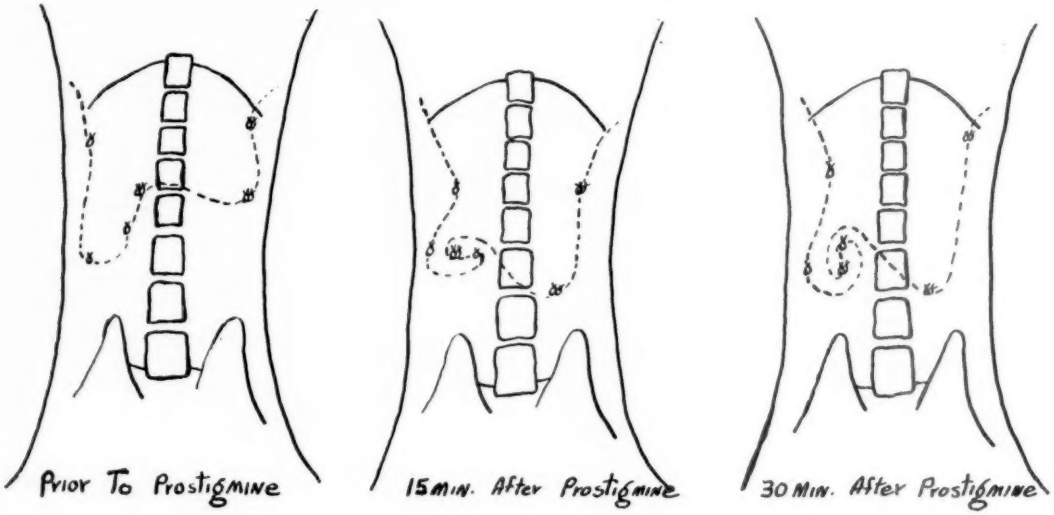

Fig. 8 (Dog 409).—Omental response to intravenous Prostigmine. Anesthetized dog secured to frame. This dog was given castor oil previously (see Fig. 7).

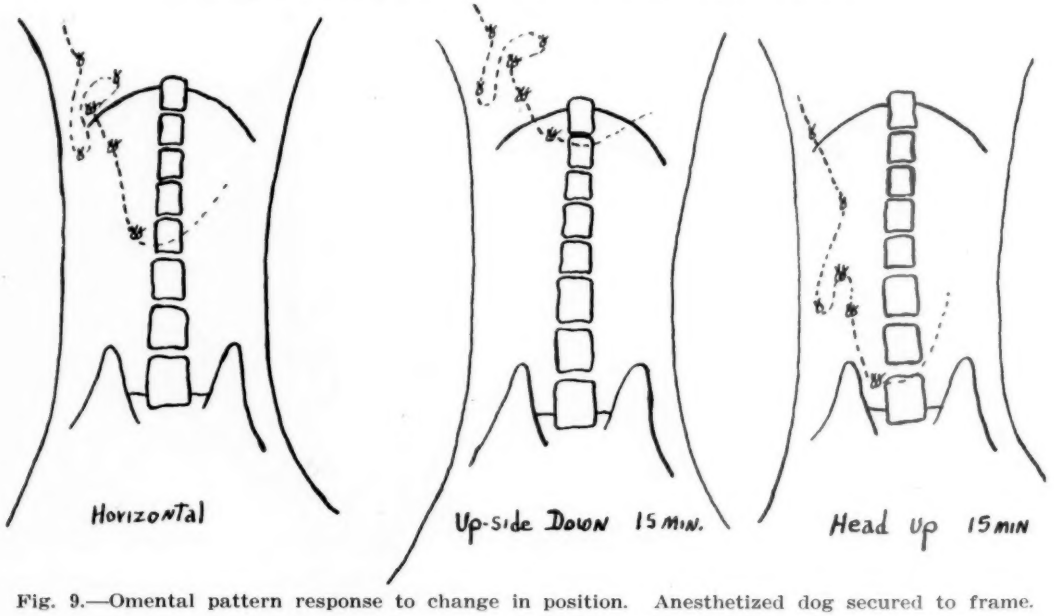

Fig. 9.—Omental pattern response to change in position. Anesthetized dog secured to frame.

The appendix of the dog is situated high in the abdominal cavity, approximately 4 cm. from the greater curvature of the stomach, in easy reach of the great omentum. In the human being at operation and at post-mortem, the omentum is often observed in the right lower quadrant adherent to an acutely

inflamed appendix or a periappendiceal mass. If the omentum were inherently "interested" in "policing the abdominal cavity"[12] and in isolating infection by forming adhesions and thus walling off the inflammatory process, it seems logical to expect a large part of its entire free border to migrate to the area of injury and enter into the protective process.

In these experiments, after anesthesia the abdomen was explored through a right lower quadrant incision. It was first ascertained that there were no omental adhesions from the previous operation. A ligature was then placed around the base of the appendix and tied sufficiently tight to obstruct the venous return. Care was taken to prevent cutting into the appendiceal wall. A No. 1 catgut ligature was used in the first three dogs and a No. 0.004 tantalum ligature was used in the latter two dogs. The abdominal wound was closed in three layers with continuous fine cotton.

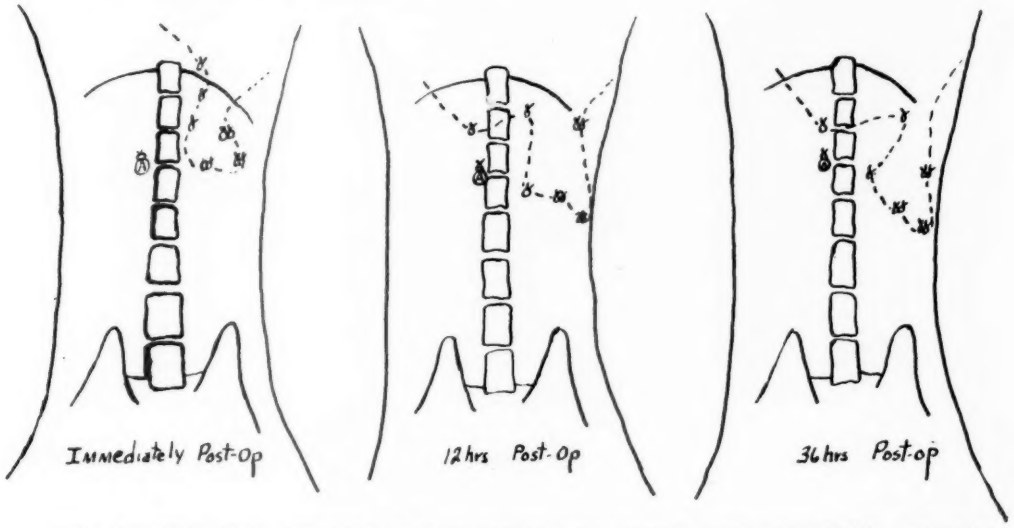

Fig. 10 (Dog 433).—Omental pattern response to experimental appendicitis. Tantalum as a ligature shows position of appendiceal base of x-ray picture. Dog died thirty-six hours postoperatively of generalized peritonitis.

Films were obtained at intervals following the surgical procedure. An autopsy was performed on all dogs. The omental pattern of Dog 433 is shown in Fig. 10. The autopsy findings in Dog 433 are shown in Fig. 11.

Results: In each dog at the time of experimental production of appendicitis, the right border of the omentum was in the same general area as the appendix. During the operative procedure there was a tendency to push the omentum up and to the left. This is reflected in the omental patterns. Roentgenographic observation of the omental pattern revealed no mass migration of the omentum to the site of injury, but the free border nearest the offending agent becomes adherent to that agent by the process of inflammation with resultant firm fibrous adhesions.

If loops of small bowel completely surround the offending agent, the omentum may become adherent to the inflammatory mass rather than to the actual offending agent, in this case a necrotic appendix. Other peritoneal

surfaces such as the mesentery of the small bowel or the mesentery of the fallopian tube may, if physically capable (being limited by their attachments), become adherent to the inflammatory mass just as readily as the omentum, and may perform a similar function in prevention of generalized peritonitis.

The failure of the omentum to become widely attached to the area of inflammation strongly suggests that any attachment which does occur is due to chance proximity of a portion of the omentum to the inflammatory process during its normal excursion already demonstrated.

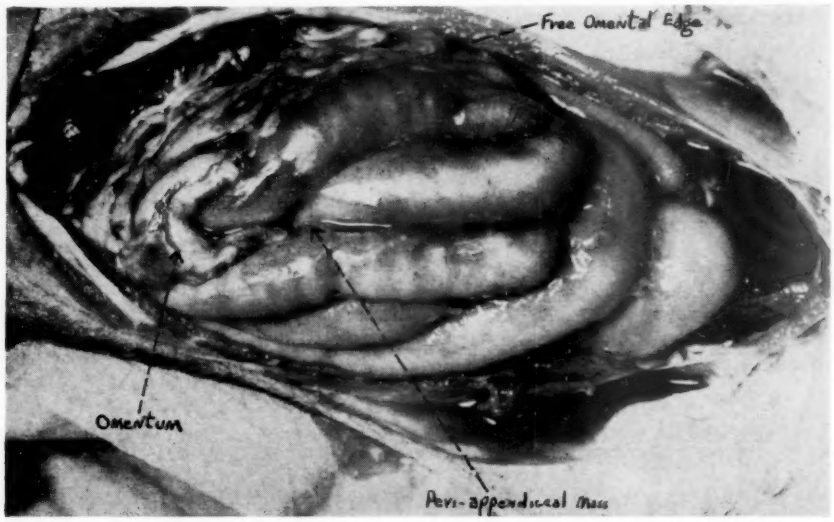

Fig. 11.—Autopsy Dog 433. Dog died thirty-six hours after ligation of appendiceal base (generalized peritonitis). Omentum in left upper quadrant of abdomen except for one small omental stalk.

Omental Pattern Response to Sterile Gauze in Right Lower Quadrant of the Abdomen.—The possibility of omental migration in response to a fixed sterile foreign body was also studied.

Five dogs with marked omenta, No. 421, 409, 407, 406, and 422, were anesthetized, and the abdominal cavities were explored through a short right lower quadrant incision. No omental adhesions were found. A small Raytex gauze sponge was sutured to the parietal peritoneum of the right lower quadrant of the abdomen, and the abdominal wound was closed. X-ray pictures were obtained at intervals. One omental pattern is presented in Fig. 12.

At autopsy there was no evidence of acute peritonitis. The gauze sponge had in each case been peritonealized in its entirety. In three dogs, this was accomplished by the parietal peritoneum, small bowel, and omentum. In Dog 421, the medial aspect of the gauze sponge had been covered by the mesentery of the right fallopian tube, and the omentum had become adherent over a small area to the medial surface of the fallopian tube mesentery. In Dog 407 the gauze sponge was covered by a loop of small bowel, including the mesentery of this loop. The omentum was attached to the resultant mass over an area of small intestine of approximately 1 by 1 by 1½ cm.

Results: Fixed, sterile foreign bodies (gauze sponges) in the abdominal cavity may be covered by intestine, mesentery of intestine, mesentery of fallopian tube, or omentum, singularly or in any combination. Mobility and position determine the part that forms the new peritoneal surface over the

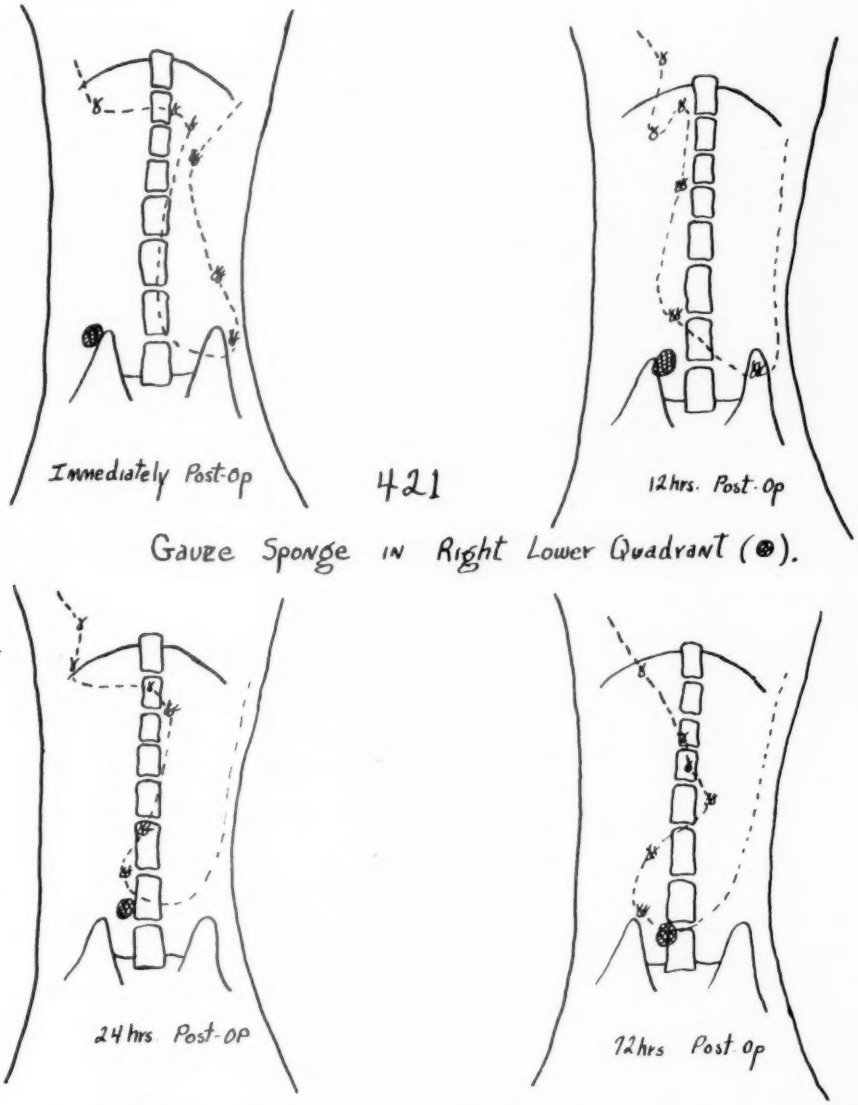

Fig. 12.—Omenta pattern response to marked gauze fixed in right lower quadrant of abdomen. Shift in position of gauze indicates shift in dog's position on x-ray table.

foreign body. Since the omentum is very mobile and since it offers an excellent surface for peritonealization purposes, it is most often involved in this reaction. However, if another part, such as a loop of small intestine with its mesentery or the mesentery of the fallopian tube, happens to make contact with the foreign body first, it too will just as readily attach itself to the foreign body and isolate it from the general peritoneal cavity.

The omental patterns reveal no massive migration of the omentum toward the foreign body; however, once the omentum comes in contact with the foreign body, its excursion away from this area is limited, as shown by the constancy of relation of one marker to the radiopaque foreign body at twelve hours and later (Fig. 12). In no instance was the entire free edge of the omentum adherent to the foreign body; in each case the edge nearest the foreign body made the initial contact and became involved in the isolation process. These results lead to the same conclusion as the observation made concerning experimental appendicitis.

Omental Migration in Response to Inaccessible Inflammation: (A) Sterile Gauze Sutured to Undersurface of the Diaphragm and (B) An Experimental Liver Abscess.—

(a) Sterile gauze sutured to undersurface of the diaphragm: In each dog in which a sponge was placed in the right lower quadrant of the abdominal cavity it was necessary to push the omentum away while the gauze was being sutured to the parietal peritoneum. In one dog, the omentum was "stuck" to the sponge before the abdominal incision was closed. This task seemed too easy for the omentum, and it was therefore decided to place the same type of foreign body in a part of the abdominal cavity that was not readily accessible to the omentum in its normal position, but which was within easy reach of the trailing omental edge if it chose to migrate in the right direction. The undersurface of the diaphragm was selected as the site.

Three unmarked dogs without previous laparotomies (Nos. 439, 440, and 441) were anesthetized, and the abdominal cavity was entered through a short epigastric midline incision. A small sterile gauze roll was sutured to the undersurface of the diaphragm above the left lobe of the liver. The abdomen was closed in layers, and each dog was returned to his cage and permitted the customary freedom of activity, food, and water. Seven days later the dogs were autopsied.

Autopsy findings: The findings were similar for all dogs and they will be described together. There was no evidence of acute peritonitis. In each case the sponge had been "walled off" or surrounded by the diaphragm, the left lobe of the liver, and the falciform ligament. In one of the three dogs (Dog 439), the sponge protruded slightly below the liver edge, and the resultant free margin was covered with fibrin. The omentum in each case was spread out over the loops of small intestine, showing no attachment to, or evidence of, an attempt to migrate toward the foreign body.

(b) An experimental liver abscess: To simulate more closely an inflammatory process, it was decided to produce an abscess in the upper surface of the left lobe of the liver and to study the omental migration response.

Two unmarked dogs (No. 422 and 443) had abdominal explorations as in the previous cases. A small stab wound was made in the upper surface of the left lobe of the liver. (This was facilitated by rotating the liver anteriorly and inferiorly from beneath the diaphragm.) A cotton pledget was soaked in a

warm fresh culture of *Staphylococcus albus* and sutured in the stab wound. The abdominal wound was closed in layers; the dogs were sacrificed on the fifth postoperative day.

Autopsy findings: There was no generalized peritonitis. The left lobe of the liver was adherent to the undersurface of the diaphragm and to the falciform ligament. The omentum was in its normal position, covering the loops of small bowel and had obviously made no attempt to migrate to the upper surface of the liver. Adhesions about the superior surface of the left lobe of the liver were separated, and an abscess cavity containing thick, white pus was encountered.

Results: An inflammatory lesion created either by the introduction of a sterile foreign body or by an experimental infectious process is walled off by the structure normally nearest it. When the area of inflammation is created at a point outside the normal range of motion of the omentum, it takes no part in the walling-off process. These experiments again indicate the chance nature of omental participation in peritoneal inflammations.

Omental Migration in Response to Occlusion of Omental Venous Return.—As noted earlier, Schutz[20] postulated that the omentum migrated in response to hyperemia or distention of its vessels as a reflex response of the omentum to peritoneal irritation. He observed a similar response experimentally after obstructing the venous return from the omentum in a normal dog.

This experiment was repeated as follows:

Three normal dogs were anesthetized, and the abdominal cavities were explored through a midline incision. The intestines and omentum were kept moist with warm saline solution throughout the procedure. All venous return from the omentum was obstructed by fine cotton ligatures. Care was taken not to injure the right and left gastroepiploic arteries and the splenic artery. The anesthesia was continued and the omentum was observed for a period of approximately two and one-half hours.

Results: There was no visible motion of the omentum other than that observed with movements of the diaphragm and peristalsis of the intestines. At the conclusion of each experiment, the omentum was slightly edematous, thickened, and congested and had occasional scattered petechial hemorrhages over its surface; however, it maintained its relative position.

It is concluded that hyperemia or distention of the omental vessels does not cause migration of the omentum.

Omental Migration in Response to Increase in Omental Arterial Pressure, Increase in Omental Blood Volume, and Dilation of the Omental Vascular Bed With Maintenance of Systemic Pressure.—Schutz[20] stated that when pressure in the omental arteries is increased, the omentum migrates. The abdominal cavities of three anesthetized dogs were explored through a midline incision. The observations were uniform in all three animals. It was observed that the omentum lay free over the loops of small bowel with no adhesions whatsoever. After heparinization, a glass cannula was placed in each femoral artery, one to record the systemic blood pressure and the other for blood donation. A

similar, smaller glass cannula was placed in the right gastroepiploic artery approximately 3 cm. from the pylorus along the greater curvature of the stomach. The small arteries and veins between the stomach and the gastroepiploic vessels were ligated with fine cotton ligatures. All cannulas contained a solution of heparin and saline to prevent clot formation. The arterial pressures in the gastroepiploic artery and in the left femoral artery were 100 mm. Hg and 120 mm. Hg, respectively. Three hundred cubic centimeters of blood was withdrawn from the right femoral artery into 50 c.c. of a heparin and saline solution. Both arterial pressure recordings dropped 30 mm. Hg but returned to normal with partial replacement of the blood volume with 150 c.c. of saline solution. By means of a T-tube connection to the gastroepiploic cannula, the 300 c.c. of blood plus the 50 c.c. of saline and heparin solution was perfused through the omental vascular tree at a known pressure of 250 mm. Hg over a period of sixteen minutes. During this time there was no recognizable migration of the omentum whatsoever. This part of the experiment was repeated three times with no change in the results. A period of stabilization was allowed before each venesection and perfusion.

Since a primary increase in pressure limited to the omental vessels created, as demonstrated, no change in the omentum, it remained to be determined whether general changes in the systemic blood pressure, which would be expected to be reflected also in the omental blood pressure, would create alteration in the omentum. For this purpose, three drugs were used, namely, (1) histamine, (2) ephedrine, and (3) amyl nitrite.

After a period of stabilization, 1 c.c. of a histamine solution on 5 c.c. of saline solution was injected into the right gastroepiploic artery. Thirty seconds later, a blood pressure fall amounting to 20 mm. Hg was recorded in both the femoral and gastroepiploic arteries. This fall gradually leveled off and the pressure returned to normal. The blood pressure curves could be superimposed. Observation of the omentum revealed no change in the gross physical appearance, and there was no indication whatsoever of a migration in its trailing edge.

Another period of stabilization was allowed, after which 1 c.c. of ephedrine sulfate solution was injected intravenously. There was an immediate parallel rise in both recorded pressures; the pressure in the gastroepiploic artery was recorded at 200 mm. Hg and the pressure in the femoral artery was recorded at 220 mm. Hg. Observation of the omentum revealed the arterial pulsation to be of greater volume, but with close observation there was no visible migration of the omental edge.

Observation of the Omentum in an Isolated Fluid Medium.—The preceding observations were confirmed by a study of the omentum in an isolated fluid medium.

In three dogs, glass cannulas were placed in both femoral arteries and in the left femoral and left jugular vein. The abdominal cavity was entered through a long midline incision, and all vessels leading to and away from the omentum were carefully ligated with the exception of the splenic artery and

vein. Care was taken to ligate the vessels near the greater curvature of the stomach to avoid injury to the gastroepiploic vessels. The latter were ligated on the right and left individually. All vessels to the spleen were ligated near the splenic capsule, and the spleen was removed. At this point the omental circulation was maintained by the relatively large splenic artery and vein.* All omental arterial pulsations appeared normal and there was no discoloration of the tissue.

After heparinization, glass cannulas were placed in the omental artery and vein (in the direction of the omentum) and were connected by means of heparinized rubber tubing to similar cannulas in the femoral artery and vein. The vessels were then severed proximal to the cannulas so that with an active circulation the entire omentum could be delivered from the abdomen and submerged in a large glass bowl containing Ringer's solution at a constant temperature of 99° F. Pressures were recorded from a T connection in the tubing between the femoral artery and the omental artery and between the femoral vein and the omental vein. The abdominal wound was closed in order to minimize exposure and shock. The circulation from the femoral vessels was adequately maintained in the transplanted omentum. Its color remained good, and arterial pulsation could be observed in the most distal omental margin.

In an effort to study the effect of omental blood flow on omental migration in the excised specimen maintained as far as possible under physiologic conditions, the following five experiments were performed:

1. Obstruction to venous return.
2. Rapid intra-arterial transfusion.
3. Perfusion of blood through the omental vascular system under a known increased pressure.
4. Dilation of the omental vascular system with maintenance of systemic blood pressure.
5. Increase in systemic blood pressure by a vasoconstrictor drug.

1. *Obstruction to Venous Return.*—This was accomplished very readily by compressing the rubber tubing connecting the omental vein with the femoral vein. The venous pressure was recorded at 80 mm. of water and it rose gradually to 200 mm. of water. The tubing was released and venous return re-established. This was repeated three times in each animal.

The omental vein near the cannula became distended as venous pressure was elevated, and the entire omental specimen moved approximately ½ cm., but in no instance was there evidence of migration of the omental edge.

2. *Rapid Intra-Arterial Transfusion.*—Rapid intra-arterial transfusion elevates the blood pressure by rapidly increasing the circulating blood volume. It was thought advisable to see if an increase in omental blood pressure and in omental circulating blood volume has any effect on omental migration.

The experimental dog was given 500 c.c. of whole blood, in a solution of heparin and saline from a donor dog, through the femoral artery not supplying

*Hereafter to be referred to as the omental artery and vein.

the omentum over a period of approximately five minutes. The arterial pressure in the omentum rose 80 mm. Hg above the normal line, with a rise in venous pressure of approximately 30 mm. of water. There was no evidence of omental migration.

3. *Perfusion of Whole Blood Through the Omental System Under a Given Pressure Increase.*—From the right femoral artery was removed 250 c.c. of whole blood, and the blood pressure was allowed to stabilize. The blood was then perfused through the omental arterial system under a pressure of 250 mm. Hg. This produced a rise in omental venous pressure to 210 mm. of water. Observation of the omentum revealed no evidence of omental migration.

4. *Dilation of Omental Vascular System With Maintenance of Systemic Blood Pressure.*—Dilation of the omental vascular system with maintenance of the systemic blood pressure was accomplished by the injection of 1 c.c. of histamine in 5 c.c. of saline solution directly into the omental arterial tree. Histamine produces capillary dilation by direct action and arterial dilation indirectly through the axon reflex.[10] This was evidenced first by a slight fall in venous pressure followed by a very slight transitory fall in arterial pressure.

There was no omental response following the intra-arterial injection of histamine.

5. *Increase in Systemic Blood Pressure by a Vasoconstrictor Drug.*—Increase in systemic arterial pressure by intravenous ephedrine sulfate is paralleled by an increase in omental arterial pressure. This pressure increase was readily recorded with the present preparation, and its influence on omental migration was observed. Following the injection of 1 c.c. of ephedrine sulfate intravenously, there was a rise in arterial pressure to the omentum to 200 mm. Hg. The pressure gradually returned to normal and the injection was repeated with a second similar rise in omental arterial pressure. Observation of the omentum throughout the experiment revealed no movement or migration of its edge.

The entire experiment produced identical results in the three dogs.

It is concluded that (1) elevation of omental venous pressure, (2) increase in omental arterial pressure and volume flow, (3) omental perfusion with whole blood under a pressure of 250 mm. Hg, (4) maintenance of systemic blood pressure with dilation of the omental vascular tree, and (5) increase in systemic blood pressure with resulting increase in omental blood pressure have no effect whatsoever on omental migration.

SUMMARY AND CONCLUSIONS

1. Tantalum wire is an excellent radiopaque, nonirritating, stable marking agent for the omentum.

2. The normal omental pattern, as shown in x-ray films after its edge had been marked with tantalum, undergoes variations of considerable degree.

3. These variations have been shown to be dependent in varying degrees on: (a) peristalsis, (b) gravity, and (c) diaphragmatic movement.

4. Migration of the omentum has no relationship to: (a) hyperemia of the omentum, (b) elevation of mental arterial pressure, (c) increase in omental volume flow, or (d) any combination of these factors.

5. The omentum is involved only in those intra-abdominal inflammatory processes which are situated within its normal range of excursion and with which therefore it might by chance come into contact.

6. The omentum reacts as other peritoneal surfaces when in contact with intra-abdominal inflammations.

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Case Reports

APPENDICITIS IN THE NEWBORN INFANT

Case Report in a Premature Infant

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Abt,[1] in 1917, published a review of eighty cases of acute appendicitis in infants under 24 months of age, thirty-seven of whom were less than 12 months old. In 1950, however, the rarity of this disease in infancy was emphasized by Abel and Allen[2] in a collection of 1,165 patients under 12 years of age, among whom only two, or 0.17 per cent, were less than 12 months old. Acute appendicitis in infants under 3 months of age is extremely rare,[3] and in the neonatal period it is seldom diagnosed before laparotomy or necropsy.[4-10] The frequency with which acute appendicitis in the newborn infant is associated with strangulated inguinal hernia has been emphasized.[5, 11-13]

Few instances of acute appendicitis have been recognized in the premature infant. Lilenthal[5] operated upon an infant 3 weeks of age, weighing 5 pounds, who was found to have acute appendicitis within a strangulated inguinal hernia sac. The patient survived. John[7] reported a premature twin weighing 2 pounds, 15 ounces who expired at the age of 20 days. Autopsy revealed acute appendicitis.

The following case report is of interest because of the patient's prematurity, weight, and survival.

CASE REPORT

G. K. (Vanderbilt University Hospital 196179), a 15-day-old premature white male twin, was admitted to the Vanderbilt University Hospital on Jan. 23, 1951, with a chief complaint of "not doing well."

Family history was not remarkable.

Past History.—The twins had a seven-month gestation and an uncomplicated delivery. The patient's birth weight was 3 pounds, 12.25 ounces; the twin's birth weight was 4 pounds, 8.5 ounces. The early condition was not known, but the patient was referred to this hospital because of his debilitated state.

Physical examination on admission revealed a small, ashen, and dehydrated white male infant who appeared critically ill. Weight was 3 pounds, 12 ounces; temperature 97.6° F.; head circumference 29.5 cm.; chest circumference 24 cm.; length 41.5 cm. The abdomen was firm and moderately distended, and the umbilicus was dry with minimal surrounding erythema. There were no palpable masses. Soft fluctuant accumulations of fluid were present on the lateral aspects of the thighs, presumably due to hypodermoclysis. The remainder of the examination was not remarkable. Prematurity and probable septicemia were the initial diagnoses.

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Laboratory Data on Admission.—Hemoglobin was 16 Gm. per cent; white blood count was 25,400. Urine was not remarkable. Blood culture revealed a light growth of *Staphylococcus aureus.*

Course and Treatment.—The patient was given constant oxygen, nothing by mouth, 20,000 units of aqueous penicillin every four hours intramuscularly, and an injection of 2.5 mg. of vitamin K (Hykinone).

On the following day, the patient's condition was unchanged. It was thought that he had cellulitis of the abdominal wall and thrombophlebitis of the lower extremities. Dihydrostreptomycin, 75 mg. every four hours, was administered intramuscularly.

The patient appeared improved during the next two or three days, and was given small amounts of skimmed milk formula through a polyethylene tube introduced into the stomach. There was no vomiting, but the abdomen remained quite firm, distended, and red. Abdominal peristalsis was audible. The stools were normal. He was afebrile.

On the fifth hospital day, he passed some bright red blood with mucus in the stools; however, the general condition seemed improved, and he was slowly gaining weight.

On the sixth day, roentgenograms of the abdomen were made because of continued abdominal distention. There was no x-ray evidence of obstruction. Dihydrostreptomycin was discontinued, and chloromycetin, 50 mg. every eight hours, was started by mouth. The accumulations of fluid in the thighs were aspirated of serosanguineous, sterile fluid.

Oral feedings were discontinued on the seventh hospital day because of occasional vomiting and abdominal distention. Hydration was maintained with parenteral fluids. The patient's general appearance, however, continued to improve.

The next day another abdominal x-ray film was obtained which revealed distention of the stomach and upper small intestines. A barium enema revealed very slow filling of the cecum and terminal ileum. The patient's general appearance was not good. His weight was 3 pounds, 12.75 ounces. Surgical consultation was obtained, and laparotomy was advised.

Through a right rectus incision, the abdomen was opened, revealing slight distention of the small bowel and a small amount of free peritoneal fluid. A peritoneal band was found stretching over the terminal ileum, and the appendix was edematous, red, and gangrenous in one area. The peritoneal band was divided, and the appendix and meso-appendix were ligated and amputated at the base without inversion of the stump. The abdominal wound was closed with through-and-through sutures of braided silk because the infant's condition was extremely poor throughout the operation.

Following operation, therapy included constant Wangensteen suction, oxygen, intravenous fluids, and whole blood. Terramycin hydrochloride,* 20 mg. per kilogram per day, was given in the intravenous drip; cortisone, 25 mg., was given, immediately followed by 10 mg. daily intramuscularly.

During the next five days, the patient was maintained on parenteral fluids. Steady improvement ensued. The abdomen became soft, and he began to pass small yellow stools. On the fifth postoperative day small amounts of electrolyte mixture† were started by gastric polyethylene tube. Parenteral fluid supplements and intravenous terramycin were continued until the seventh postoperative day. On the eighth postoperative day, the patient was able to take formula from a nipple. Cortisone dosage was diminished at the end of the second week postoperatively.

The postoperative course was complicated by *Staphylococcus aureus* septicemia on two occasions; these occurred during the sixth and tenth postoperative weeks. The patient was treated with penicillin, terramycin, and chloromycetin, and received several small whole blood transfusions. He also developed bilateral inguinal hernias and small herniations along the line of abdominal incision.

He continued to thrive and gain weight, and was discharged from the hospital weighing 7 pounds, 4 ounces. The total length of hospitalization was sixteen weeks.

*Manufactured by Chas. Pfizer and Co., Inc.
†Meade's No. 297.

Since discharge he has been followed in the outpatient department, and was gaining weight and doing well when last seen at the age of seven months.

COMMENT

Treatment of acute appendicitis in the neonatal and infancy periods requires the combined cooperation of the pediatrician and surgeon, for the disease in this period presents problems which are extremely formidable. These problems result from the following facts:

1. Perforation of the appendix is likely to occur early because of the infant's poor response to the infection.

2. Generalized peritonitis is common, for the role of the greater omentum in localizing the infection is not adequate.

3. Clinical signs and symptoms may be misleading because of the rarity of the condition in this age group.

4. The operative procedure requires meticulous handling of delicate and diseased tissue.

5. Postoperative management necessitates almost constant observation of the patient and an exacting regulation of the patient's fluid balance and nutrition.

SUMMARY AND CONCLUSIONS

1. Acute appendicitis in the neonatal period is extremely rare, but must be considered in differential diagnoses of intra-abdominal disease, particularly when vomiting and abdominal distention are present.

2. Adequate treatment of these patients requires the combined care of the pediatrician and the surgeon.

3. An instance of acute appendicitis is presented in a premature infant who survived.

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LARYNGOCELE: AN UNUSUAL TUMOR OF THE NECK

Case Report

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In 1947, McLaurin[10] found approximately forty cases of laryngocele reported in the literature. However, most of the reports concerning this unusual tumor of the neck appeared in the specialized literature of otorhinolaryngology,[6, 8-10, 12, 14] and a review of the literature revealed that this lesion was rarely included in the differential diagnosis of tumors and cysts of the neck.[1-5, 7, 11, 13]

CASE REPORT

A 29-year-old white male brewmaster's apprentice was referred to the Surgical Service in December, 1951, for investigation of a mass in the left side of the neck. He stated that he had first noted a swelling in the neck in 1947 and concurrently had begun to have recurrent episodes of sore throat and dysphagia. There was no hoarseness or dyspnea. The patient had been told that the swelling was caused by recurrent tonsillitis and a tonsillectomy was performed, but without relief of symptoms. The patient received no further treatment prior to our consultation. During the intervening period, the swelling gradually increased and the episodes of dysphagia and sore throat occurred more frequently. The patient noted that when he sang loudly, the mass became more prominent or increased in size. External pressure on the mass was not painful and had never caused a hissing sound in the throat. There was no history of external drainage from the neck.

Examination revealed a soft, movable, nontender, cystic mass lying in the anteromedial border of the sternocleidomastoid muscle in the upper third of the neck. The mass measured 5 cm. in its greatest diameter. There was no surrounding induration, enlargement of the thyroid gland, or cervical adenopathy. The mass did not move with swallowing. All laboratory studies were within normal limits.

A diagnosis of left branchial cleft cyst was made, and on March 19, 1952, exploration was carried out under endotracheal anesthesia through a transverse incision across the mass. The mass was exposed by retracting the sternocleidomastoid muscle laterally and the strap muscles medially. It appeared to be a unilocular cyst about 5 cm. in diameter, with a thin, rubbery, translucent wall. A narrow stalk was found posteromedially which extended behind the strap muscles and entered the lateral thyrohyoid membrane. The cyst was aspirated, and air, but no fluid, was recovered. The stalk was transected at the base and a probe inserted through its lumen into the larynx. The base of the stalk was inverted with interrupted fine chromic sutures, and the small defect in the thyrohyoid membrane was reapproximated over the inverted stalk. A small Penrose drain was placed down to the thyrohyoid membrane and was brought out through the lateral end of the incision. The remainder of the wound was closed in layers with interrupted sutures of fine cotton. Microscopic examination of the sac revealed a lining of ciliated pseudostratified columnar epithelium (Fig. 1).

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Fig. 1.—Microscopic section of laryngocele, showing ciliated pseudostratified columnar epithelium.

Fig. 2.—Lateral cervical film showing air-filled sac. (From Taylor.[14])

The drain was removed twenty-four hours after operation. Penicillin and streptomycin were given parenterally for four days. The patient recovered uneventfully and was discharged seven days after operation. Three months after operation he was asymptomatic, and direct laryngoscopy and roentgenograms of the neck revealed no abnormalities.

DISCUSSION

The differential diagnosis of tumors and cysts of the neck, as considered by most authors,[1-5, 7, 11, 13] has not included laryngocele. In 1947, Jackson[6] briefly reviewed the history and incidence of laryngocele. He defined the lesion as a "hernia of the larynx" and reiterated that the air sac connected with the larynx usually arises in the laryngeal ventricle. Most authors[6, 9] mention two or three types of laryngocele. The internal type is contained within the thyroid cartilage. The external type pierces the thyrohyoid membrane and presents itself externally as a tumor of the neck. Jackson[6] quoted Leborgne as stating that the laryngocele may be associated with laryngeal carcinoma in 10 to 15 per cent of the cases. Lathrop[8] reported purulent inflammation complicating two cases of laryngocele (laryngopyocele). Lindsay[9] observed changes in the size of the sac with intralaryngeal pressure change by the use of planograms. He discussed increased intralaryngeal pressure as the generally accepted etiology of this lesion.

Hoarseness is the most common symptom,[6, 10] but it was not noted by this patient. Often, patients note that pressure over the mass elicits a hissing sound in the larynx.[6] Again, this patient was an exception. Dyspnea occurs only if an intraglottic (internal) component causes obstruction. Coughing, singing, or any rise in intraglottic pressure usually enlarges the external mass.[9] Examination should include direct laryngoscopy to note the presence and size of any intraglottic component and to rule out associated papilloma or carcinoma of the larynx.[12] The importance of routine neck films for examination of neck tumors is emphasized by this lesion, for an x-ray picture usually establishes the diagnosis by demonstrating an air-filled sac (Fig. 2). Diagnostic aspiration of the cyst or tumor, with its risk of introducing infection, is thus avoided.

Treatment is by excision.[6, 10] Attention should be paid to careful inversion of the base of the transected laryngocele stalk. Whenever possible, the defect in the thyrohyoid membrane should be reapproximated, in an attempt to prevent recurrence.

SUMMARY

A case of superior external laryngocele is presented. Diagnosis and treatment are discussed, and a brief review of the literature is included. It is recommended that differential diagnosis of neck cysts and tumors include this unusual lesion.

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MESENCHYMOMA

Report of a Case

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THE mesenchymoma has been recognized and described as a tumor entity by Arthur Purdy Stout who referred to it as a "neoplasm composed of an admixture of two or more nonepithelial mesenchymal derivatives that ordinarily are not found together in a single tumor." To quote Stout again in this connection, he stated that "mesenchyme is an extremely versatile tissue, which in ordinary development produces the normal prototypes of all of the tissues of which these malignant cells are the grotesque caricatures."

The primitive mesenchymal cell endowed with amazing growth energies is the ultimate ancestor of the various tumors of the soft somatic tissues, both benign and malignant. In the ordinary course of differentiation these mesenchymal cells finally emerge into specific functional tissues such as fat, muscle, fascia, nerve, synovia, and so forth, but seldom in pure form because of the variable proportions of stromal elements which are present. The connective or fibrous tissue component of the somatic tumors may constitute a relatively small proportion of the neoplasm as in some liposarcomas or a major part of the bulk as in some malignant synoviomas. The preponderance of connective tissue in some sarcomas has led to the erroneous appellation of "fibrosarcoma" without due consideration of the histogenesis of the more differentiated type cell, which is present but less conspicuous. The term mesenchymoma as employed by Stout excludes from the classification any tumor in which one of the two elements is fibroblastic, and rightly so because fibroblasts can be elaborated by synovial cells and others. Also excluded are tissues of metaplastic change, such as the occurrence of bone in a liposarcoma or the development of sarcoma in myositis ossificans.

The mixed mesenchymal tumors are comprised of two or more somatic tissues of different histogenesis in addition to the variable proportions of fibrous stroma present. Theoretically, the mesenchymomas should be frequent instead of rare. The neoplasm may contain adipose, angiomatous, osseous, cartilaginous, hematopoietic, myxomatous, and smooth muscle tissues, but such multiple admixtures are seldom found. Each of the component tissues may be as fully malignant as any sarcoma of pure histogenetic type. The potpourri of tissues varies widely in composition and in degree of malignancy. In lieu of the term mesenchymoma, implying a malignant tumor, compound terms have found some usage in medical literature, but Stout's identification of them in the single category is a definite titling which should be adopted. Some of the sarcomatous elements are in greater proportion than others; therefore, there is no set pattern of composition.

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Although Stout admitted that metaplasia may play a role in the genesis of these tumors, he was inclined to consider them largely as dysontogenetic neoplasms, originating as developmental aberrations. An argument in favor of metaplasia, he pointed out, is the possible occurrence of heterotopic bone and cartilage, whereas in substantiation of the dysontogenetic theory is the occurrence of mesenchymomas in regions where congenital abnormalities are found.

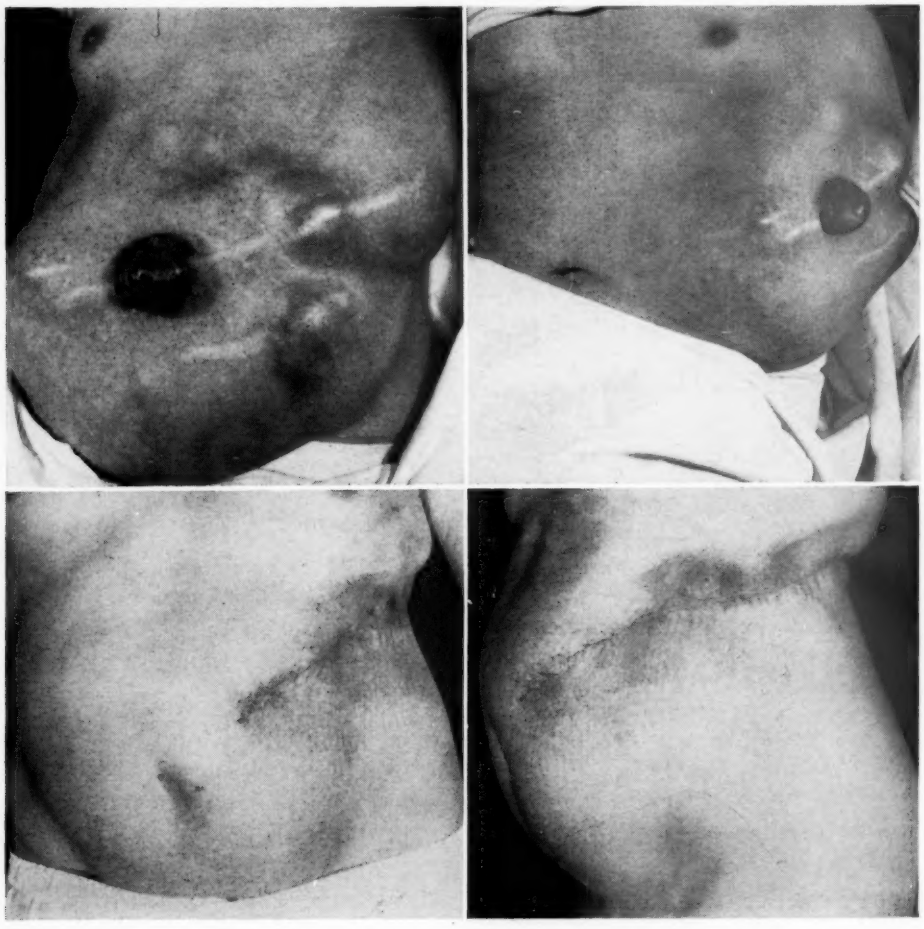


Fig. 1.—*A*, Clinical photograph of mesenchymoma, anterior view. Note nodularity and bulk of tumor. It involves both abdominal and thoracic walls.
B, Another view illustrating lateral protuberance.
C, Postoperative photograph after removal of large segment of abdominal wall, costal margins, portions of diaphragm, and pericardium.
D, Photograph showing defect after it was closed by tantalum mesh and skin.

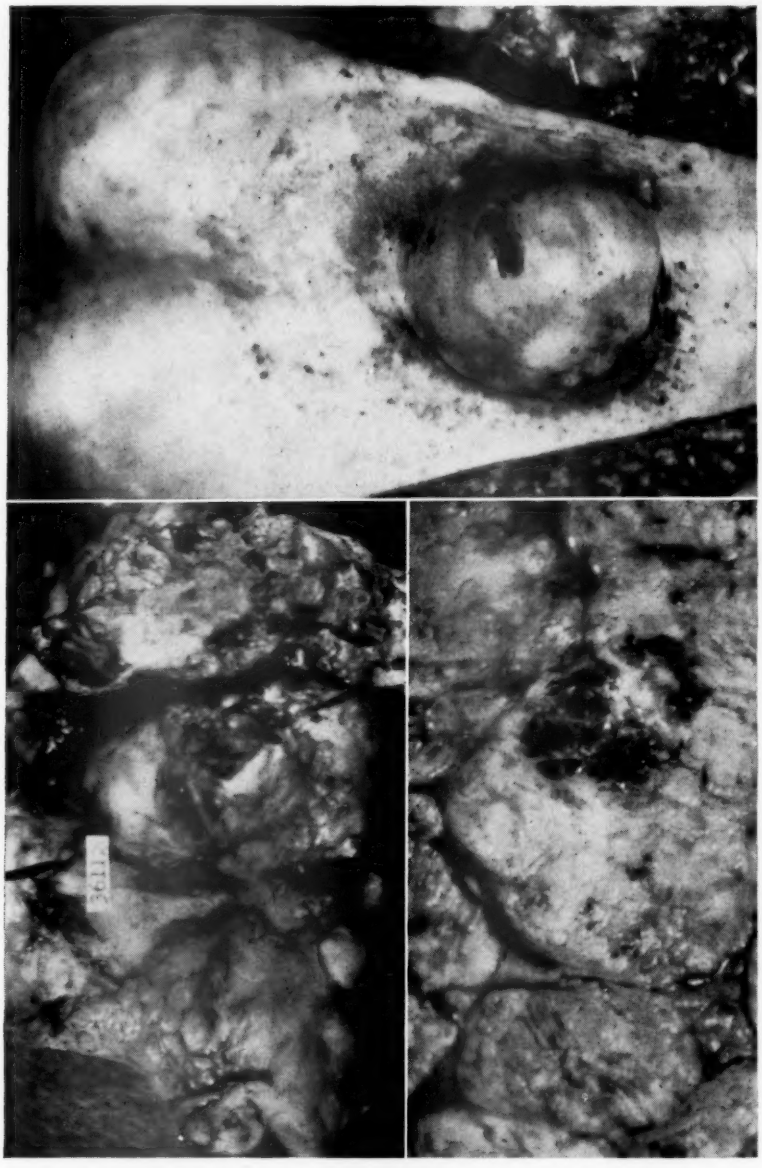
The proper treatment is radical surgical excision with ruthless sacrifice of the containing tissues, viscus, or extremity. Radiation therapy may secure a palliative end result of variable duration, but cure by such treatment would not be anticipated.

CASE REPORT

C. K., a 54-year-old white man, was first seen on Oct. 14, 1949. In May, 1949, he had observed a lump in the left upper anterolateral abdominal wall, which tumor was re-

sected at St. Joseph's Hospital, Paterson, N. J. on May 19, 1949. At that time, portions of the ninth and tenth ribs were removed. Within two months, a recurrence had developed in the medial aspect of the incision involving the abdominal wall. X-ray therapy had been given without apparent effect. Weight was maintained at 208 pounds.

A.



B. *C.*

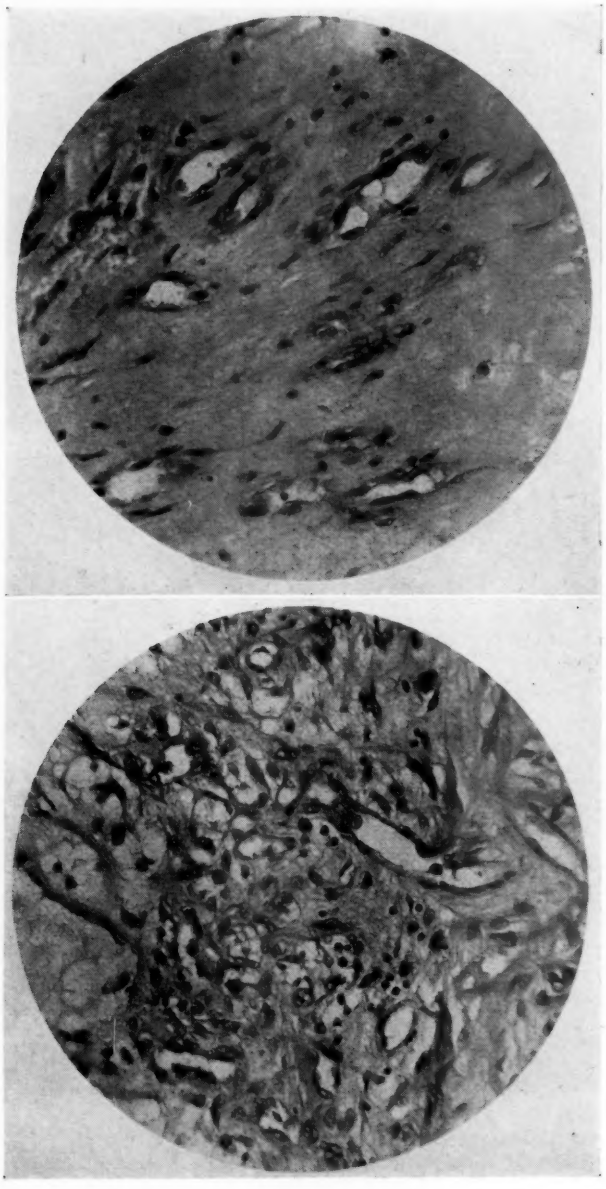
Fig 2.—Photographs of mesenchymoma showing the external nodular appearance of the skin (upper), the nodular appearance of the undersurface (lower left), and the cut surface (lower right).

At the time of our first examination, a fungating recurrent sarcoma was seen to involve the left lower anterolateral chest wall adherent to and involving the ribs. It was fixed and immovable. A roentgenogram of the chest revealed evidences of pulmonary metastases. Posterior-anterior and left lateral x-ray films of the chest showed densities in the

lower portion of the right lung field in the posterior gutter. There were no axillary or lymph nodes palpable at the time. On fluoroscopy, the diaphragm moved well, and on physical examination, ventilatory excursion was adequate and the patient had good respiratory reserve.

The patient refused surgical intervention and went to a tumor hospital in Philadelphia. While there, he received fractionated treatments with polysaccharides at monthly

A.



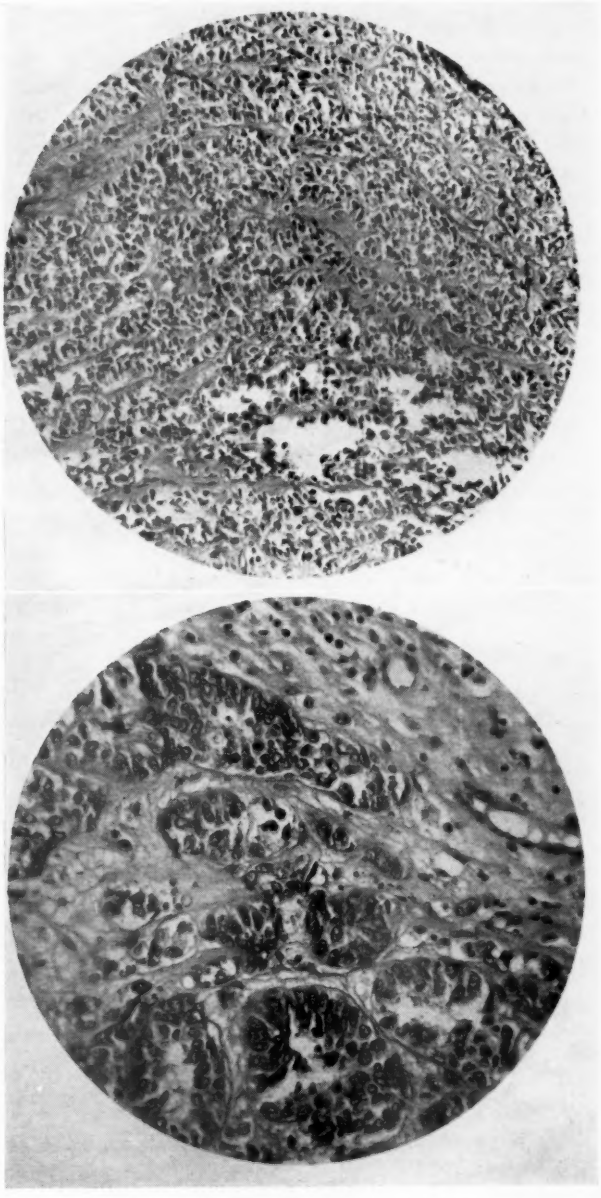
B.

Fig. 3.—*A*, Photomicrograph of the vascular channels which are lined by endothelial cells showing moderate anisocytosis and hyperchromia. They merge into the surrounding tissue which has a few cells of similar nature. There are foci of necrobiosis. (×200, reduced ⅓.)

B, Photomicrograph showing more marked vascularity. The endothelial cells display a greater degree of anisocytosis and the surrounding tissue is richer in neoplastic elements. (×300, reduced ⅓.)

intervals, starting on Nov. 30, 1949, and continuing until April 16, 1951. During this time, the recurrent tumor of the chest wall tripled in size; when he returned in May, 1951, the huge fungating tumor was as shown in Fig. 1. In the meantime, the patient had lost considerable weight. The roentgenograms of the chest now showed the pulmonary metastases to be much larger than at previous times.

C.



D.

Fig. 3 (*continued*).

C, Photomicrograph showing how the richly cellular area closely simulates epithelial structures. Other foci reveal primitive chondroblasts. (×70, reduced ⅓.)

D, Photomicrograph showing the neoplastic cells arising directly from the wall and producing solid nests which fill the channels. There is marked anisocytosis and hyperchromia. Mitoses are present in moderate numbers. There are a few inflammatory cells. (×300, reduced ⅓.)

On June 11, an operation was performed by making an incision along the course of the twelfth rib with extension inferiorly and medially toward the midportion of the abdominal wall. The skin was then dissected away from the mass and, by encompassing the contours of the tumor, the musculature of the abdominal wall which had become extremely frayed was dissected away from the mass. The external oblique, transversalis, internal oblique, and left rectus muscles were transected, and in one portion of the abdominal wall, where the tumor had infiltrated these muscles and the peritoneum, it was necessary to excise all of these structures, leaving a huge defect in the abdominal wall. As the dissection progressed superiorly, it was necessary to resect the lower three ribs, after which the intrathoracic portion of the mass was excised by removing a portion of the pericardium and a large segment of the left leaf of the diaphragm. Numerous implants of the tumor were noted within the substance of the lung, on the diaphragm, and on the parietal pleura.

After the huge tumor mass had been dissected free from the body wall and removed, the resultant defect was repaired by suturing the diaphragm to the chest wall at the level of the ninth rib. The chest wall was then closed with interrupted silk sutures, and a drain placed under water. The abdominal cavity was closed by suturing the peritoneum and the remaining abdominal musculature in the four quadrants of the defect to each other, leaving a central defect 10 cm. square, which was repaired by suturing a tantalum mesh in place, over which the skin was approximated. The tantalum mesh was in direct contact with the viscera and was the only structure intervening between the subcutaneous fat and the viscera.

Convalescence was completely uneventful. The wound healed well. The patient gained twenty pounds in weight after the operation, and the metastases in the lungs remained relatively quiescent. Six months later, pleural effusion developed requiring thoracentesis. He died ten months after the date of operation. The period of complete palliative relief was approximately six months.

Gross Pathologic Anatomy.—The tumor was a huge, grossly nodular mass measuring 34 by 23.5 by 11.8 cm. and covered by a triangular segment of skin with a healed central surgical scar. The mass was divided into lobules of milky-white or yellow-white firm tissue with occasional hemorrhagic foci. It was tightly adherent to the periosteum of the rib segments (Fig. 2).

Histologic Features of the Tumor.—The neoplasm was extremely vascular. Within the tumor could be seen thin-walled blood vessels lined by neoplastic endothelial cells lying in a relatively loose tissue which had a few necrobiotic foci (Fig. 3, *A*). Other portions were much richer in blood vessels and lay in tissue which had the same type of cell as that which lined the vessels. Other segments of the neoplasm (Fig. 3, *C*) were much more cellular, and some foci resembled primitive cartilage. These channels were lined by malignant cells similar in character to those of the other areas but displayed more anaplasia and anisocytosis. A moderate infiltration by inflammatory cells was present.

Diagnosis.—Diagnosis was mesenchymoma of thoracoabdominal wall.

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CONGENITAL DUPLICATION OF THE GALL BLADDER

Review of the Literature and Report of an Unusual Symptomatic Case

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CONGENITAL duplication of the gall bladder is quite rare. From a review of this and other types of gall bladder malformation, it would appear that the incidence of gall bladder anomalies is considerably less than that of other segments of the extrahepatic biliary system.[21] Furthermore, gall bladder anomalies, when symptomatic, do not become so until adult life in contrast to the frequency of neonatal symptoms, generally obstructive jaundice, accompanying anomalies of the hepatic and common bile ducts.

Because of the wide range of variations in size, shape, and location encountered in the recorded cases of gall bladder duplication,[10, 20] it is desirable to classify these malformations only within rather broad limits. Accordingly, a duplication may be regarded as either a complete or a partial one. In the cases of complete duplication, the "vesica fellea duplex" group of Boyden,[5] the two gall bladders do not communicate and may or may not have separate serosal coverings. Furthermore, in these cases the cystic ducts may be completely duplicated, entering the common duct each with its own orifice, or they may be only partially duplicated, joining at a "Y" junction with a single opening into the common duct.

The gall bladder may be bilobed or partially septate in cases of incomplete duplication, Boyden's "vesica fellea divisa" classification. Only a very few instances, approximately eight in number, of incomplete duplication have been reported,[20] and it is with the occurrence of complete duplication that this study will be largely concerned.

Thirty-five cases of complete duplication of the gall bladder, proved either by operative or necropsy examination, have been reported up to the present time.[2-4, 5-15, 17-20, 22-39] Unconfirmed cases in which the diagnosis was based solely on roentgen interpretation have been excluded. The first case of complete duplication to be discovered on post-mortem examination was described in 1674 by Blasius.[4] Yet, it was not until 1911 that Sherren[31] reported the first discovery of this singular malformation at operation.

Because of the rarity of gall bladder duplication, it has seemed desirable to report an unusual symptomatic case in which there was complete duplication of both the gall bladder and cystic duct, each gall bladder having a separate serosal covering, and in which one gall bladder was normal and the other acutely inflamed.

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CASE REPORT

The patient, a 30-year-old white woman, was admitted to the hospital on May 9, 1951, because of severe right upper quadrant abdominal pain of twelve hours' duration. The pain was referred to the tip of the right shoulder and was associated with nausea and vomiting. She had had five similar attacks during the two years prior to admission, and complained of intolerance to fatty foods. There was no history of jaundice.

Physical examination revealed epigastric and right upper quadrant tenderness. The findings otherwise were within normal limits. The red blood count was 4.2 million and the hemoglobin 13 Gm. The serology was negative and the urine normal. White blood count was 16,200 with 83 per cent neutrophils. The serum amylase level was 94 Somogyi units. On May 11, cholecystography demonstrated a normal functioning gall bladder (Fig. 1). The symptoms subsided and the patient was discharged from the hospital May 12.

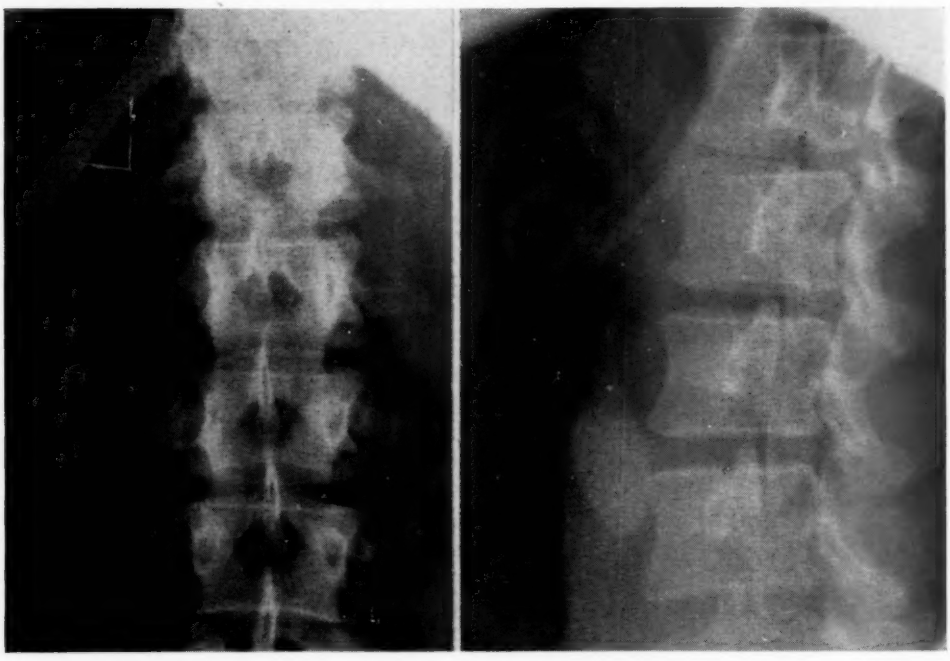

Fig. 1.—Anterior-posterior and lateral films showing cholecystographic evidence of normal function of one of the gall bladders, presumably the normal-appearing distal one.

She remained relatively asymptomatic until she was readmitted to the hospital on Jan. 20, 1952, with a recurrence of the severe right upper quadrant abdominal pain of three days' duration. The pain was again associated with nausea and vomiting, and she had not been jaundiced. In addition to right upper quadrant tenderness, a mass was palpated just below the right costal border. The red blood count was 4.4 million, the hemoglobin 14.5 Gm., and the white blood count 8,800. The Bromsulphalein test demonstrated normal excretion of the dye. The fasting amylase was 133 units and the Prostigmine amylase test levels were within normal limits. Cholecystography again revealed a normally functioning gall bladder. Despite roentgen evidence of an apparently normal gall bladder, it was felt that a right upper quadrant exploration should be carried out.

On Jan. 23, under cyclopropane anesthesia, the peritoneal cavity was opened through a right subcostal Kocher-type incision. On examination of the extrahepatic biliary system, two well-developed and separate gall bladders were found (Fig. 2). Each gall bladder had its own serosal covering, and the cystic ducts were completely duplicated. The distal

gall bladder had a smooth, glistening serosal covering and appeared to be normal in every way. The proximal gall bladder, on the other hand, was red, tense, and edematous, and its serosa had a dull, granular appearance. Stones could not be palpated within either structure or within the hepatic or common bile ducts. Because of the normal appearance and the apparently normal functional capacities roentgenologically of the distal gall bladder, it was decided to leave this organ intact and to remove only the acutely inflamed proximal gall bladder. This was accomplished by dissection of the proximal gall bladder from above down. The cystic duct was ligated and divided near its junction with the common duct, and a Penrose drain was placed down to the site of removal. The wound was closed in layers. No stones were found when the excised gall bladder was opened. Nevertheless, evidence of acute inflammation was found on microscopic study.

Fig. 2.—Drawing of the appearance, at operation, of the two gall bladders and their cystic ducts.

The postoperative course was uneventful, and the patient was discharged from the hospital on Jan. 26. Since her release from the hospital, she has had no recurrence of abdominal pain and has been otherwise free of symptoms.

DISCUSSION

Although gall bladder duplications are exceedingly rare in human beings, there is a rather high incidence of them in other animals. This fact accounts for a considerable historical interest in gall bladder anomalies which can be

traced to ancient times. This interest, to be sure, derives principally from the frequent discovery of these anomalies in sacrificial animals.

Jastrow,[16] in a comprehensive study of the religion of the Babylonians and Assyrians, cited some forty cuneiform texts dealing with gall bladder malformations. A similar interest is to be found in Hebrew literature pertaining to the certification of kosher meats.[5] The finding of gall bladder anomalies also was regarded by the ancients as being of some prophetic significance. In this regard, Pliny considered worthy of mention the finding of a double gall bladder in a sacrificial animal on the day of the great naval victory of Octavianus Caesar over the combined forces of Anthony and Cleopatra at Actium (31 B.C.).

Because of his apparently significant incidence of gall bladder duplications in some animals, Boyden attempted to determine the incidence of this abnormality in certain animals by examining large numbers of them. He found that partial or complete gall bladder duplication occurred once in every eight cats examined and in a ratio of 1:28 in calves, 1:85 in sheep, and 1:198 in pigs. Only 7 per cent of the duplications in cats were complete, whereas 52 per cent of those in calves were. In a few animals, multiple duplications were encountered.

In human beings, on the other hand, complete duplication of the gall bladder is quite uncommon, only thirty-six instances, including the one herein recorded, having been reported up to the present time. The anomaly was encountered as an incidental necropsy finding in nine of the cases, and in twenty-seven, the discovery was made at the time of operation, generally for symptoms suggesting gall bladder disease. As pointed out by Gross,[10] this finding might appear to suggest that the majority of gall bladder duplications ultimately become symptomatic.

The ages of the patients with symptomatic duplications ranged from 19 to 69 years, and averaged 43 years. Eighteen of the patients were women and six were men. Information was available concerning the cystic ducts in twenty-nine cases. In twenty-two cases, they were completely duplicated, entering the common duct at separate orifices, while in seven cases, they were found to join at a Y junction with a single opening into the common duct.

Although considerable variation in the size and location of the two gall bladders has been described, the commonest single form of the malformation appears to be side-by-side occurrence, with a common serosal covering. For this reason, the existence of the duplication in a few cases was not established until the surgical specimen was examined. Occasionally, the gall bladders may be more widely separated, as they were in the case reported by Wischnewsky,[37] in which one gall bladder was located to the right and one to the left of the falciform ligament. In the interesting case reported by Croudace,[7] the cystic duct from one gall bladder entered the common bile duct, whereas the duct from the accessory gall bladder passed directly into the liver.

Symptoms accompanying gall bladder duplication are, as a rule, those of cholecystitis, generally secondary to cholelithiasis involving one or both of

the gall bladders. Cholecystitis has been discovered in a few instances in the absence of cholelithiasis. In one case, the inflammation was due to parasites[2] and in another, obstructive cholecystitis was found to be due to hypertrophied tissues, resembling Brunner's glands, at the ampulla of one of the gall bladders.[31] In the case reported here, no clear cause of the acute cholecystitis was demonstrated. In the case reported by Recht,[27] symptoms resulted from volvulus and gangrene of one of the two gall bladders. The cystic ducts joined at a Y junction in this case.

Although roentgenographic demonstration of gall bladder duplication is possible either from the identification of two separate areas containing gallstones or the visualization of two functioning gall bladders on cholecystography, the findings may also prove misleading.[1] The establishment of this diagnosis depends, to be sure, on operative or necropsy identification of the duplication.

The surgical management of symptomatic cases of gall bladder duplication is, in essence, the management of cholecystitis and cholelithiasis. The diseased organ or organs should be removed. Since both gall bladders are generally diseased, and since they are often rather intimately attached to one another, it is seldom possible to excise an abnormal gall bladder and leave a normal one. The case reported here is unusual in that separation of the two gall bladders made it possible to remove the acutely inflamed proximal one and leave undisturbed the normal-appearing distal one which had previously been shown to function normally on cholecystography. This approach has been possible in only two other reported cases of this malformation. In the case reported by Wischnewsky,[37] the acutely inflamed gall bladder to the left of the falciform ligament was excised and the normal one to the right of the ligament was left intact. Recht's[27] case of a volvulus of an accessory gall bladder with gangrene was treated by removal of only the accessory organ. Although the experience with this anomaly is, as yet, too small to permit any rigid conclusions, there seems to be no impelling reason to excise the normal one of duplicated gall bladders when it can be left behind with apparent safety. Furthermore, there does not seem to be any clear indication for operating upon patients with asymptomatic gall bladder duplication, even though initial impressions might be interpreted as suggesting that there may be a greater tendency for duplicated gall bladders to be affected by cholelithiasis and cholecystitis than nonduplicated ones.

SUMMARY

1. The literature pertaining to congenital duplications of the gall bladder is reviewed, and the classification of these malformations into complete and incomplete duplications is discussed.

2. A symptomatic case of complete duplication of both the gall bladder and cystic duct is reported. Each gall bladder had a separate serosal covering. The proximal gall bladder was acutely inflamed and was removed. The distal one was normal in appearance and had been shown to function normally

by cholecystography. It was left behind. Neither gall bladder contained stones.

3. Thirty-six cases of complete duplication, including the one herein recorded, have been reported up to the present time. Of this number, nine were discovered at post-mortem examination and twenty-seven at operation.

4. In the vast majority of cases, the symptoms have been those of cholecystitis and cholelithiasis. Seventy-five per cent of the patients have been women, and the age of onset of symptoms has ranged from 19 to 69 years, with an average age at onset of 43 years.

5. In approximately 75 per cent of the cases of complete duplication of the gall bladder, the cystic duct has also been completely duplicated. In the remaining cases, the cystic ducts have joined at a Y junction and have entered the common duct with a single opening.

6. Although it has occasionally been possible to remove a pathologic gall bladder and leave a normal one, the surgical management in the majority of symptomatic duplications has involved the removal of both gall bladders, either because both were diseased or because their relatively intimate approximation prevented selective removal.

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Editorials

The Research and Development Board

ON JUNE 30, 1953, the Research and Development Board ceased to exist. Instead, its functions are now under an Assistant Secretary of Defense in charge of Research and Development. This announcement probably meant very little to the vast majority of persons in the medical profession, yet since 1948 this Board has advised the armed services in their research programs and has endorsed, increased, or decreased vast amounts of money for this purpose. Several of the committees of the Board had intimate association with medical affairs: atomic energy, biologic warfare, chemical warfare, human resources, and medical sciences, for example, and others somewhat more remotely.

"The committees function in broad technical fields to assist the Board in providing constructive guidance for the research and development activities of the Department of Defense."

The committees in turn appointed numerous panels: "Panels function in specific technical fields to assist committees in carrying out their responsibilities."

How the new organization will operate has not yet been officially determined. As one who has been intimately associated with the Panel on Military and Feld Medicine and also with the Committee on Medical Sciences since 1948, I want to take this opportunity to point out how this civilian group works with the services. True, the Committee on Medical Sciences overlapped other committees, made contact with the Armed Forces Medical Policy Council, and stretched out into the development of engineering devices and matériel, into the Quartermaster Department concerning clothing and its protective cooling effects in cold and hot climates, into the food laboratory in Chicago under the Quartermaster Department, and into the entomologic laboratory in Orlando, Fla., under the Department of Agriculture, with its important role in preventive medicine and public health.

The machines invented by man have now become so complicated and fearsome that some are well ahead of man's ability to cope with them. Therefore, we have a real interest in human engineering. These problems are being studied both from research and practical application at the Special Devices Center of the Navy and in the laboratories of the Air Force and the Naval Air Arm. In particular, the research of the Marine and Army laboratories has brought about revolutionary changes in the types and proportions of serious chest and abdominal wounds by the development of lightweight protective armor, which has met with such notable success in Korea concerning both protective and morale factors. The results have been a marked decrease in serious

chest and abdominal wounds and a corresponding increase in multiple extremity wounds with the saving of lives. Building on these foundations and the report by the Board for the Study of the Severely Wounded in the North African Mediterranean theater of operation, surgical research teams are at work both in the field and laboratories of Korea and Japan and in the larger hospitals in this country, carefully studying and recording the altered physiology of the wounded, various and improved techniques in vascular repair and plasma expanders, the use of whole blood as carried forward by helicopters, and extensive studies in the treatment of burns.

These are but a few of the problems that are now the active concern of the medical departments of our armed forces, and all are of prime interest to the surgeon. Each year, members of the Committee have made a short tour of some of the laboratories and facilities where this work is being carried out, and some have also visited the battlefields of Korea and the hospitals and laboratories of Japan. It is essential that the armed forces maintain this program of research and that their work be expanded by further studies in their own hospitals and also through contracts with various medical schools and hospitals throughout the country. This research in human engineering and in many of the problems associated with trauma, mass casualties, and evacuation can only be performed by the services. They are our representatives and, as such, need the cooperation and help of each and all of us. What impresses one when traveling about, however, is the difficulty they operate under in the sense of continuity of personnel in problems of research. Except for the purely laboratory workers, a career pattern in research is difficult to assure, but this is necessary if worth-while and constructive research is to be performed, otherwise there will be mere repetition. This was evident in a recent tour of various facilities by members of the Committee on Medical Sciences. We found almost universal satisfaction with the assignments of personnel and considerable enthusiasm. On the other hand, it was evident that some ground was being replowed that had been tilled before.

Since the creation of the Board in 1948, there has been a steady increase in coordination, sharing of information, and joint participation in and sharing of benefits derived from the various research projects. Each service knows what the other is doing, and unnecessary duplication is gradually being eliminated. We on the civilian side can be of real assistance by scrutinizing closely and evaluating carefully our own research programs so as to be sure that they are not mere schemes to obtain easy money from the services.

Whether we like it or not, we are apparently in a state of expanded military activity on a semipermanent basis, so we had best make the most of it and use the opportunities afforded for the training of interns and residents during their tour of duty in the armed services. There is no reason why the various boards, for example, should not allow basic science, research, or laboratory credit for at least part of the time spent by the group of young men who are on these assignments. Many are doing just as good work with equally good leadership and as ample opportunities as they have in our own civilian

hospitals for a similar period in their training. Furthermore, those in the armed services who are responsible for and in charge of the research programs will welcome sincere interest and suggestions from the civilian profession in helping carry forward this program so that it may bring true progress and not just change.

—*Frank B. Berry*

Cardiac Arrhythmia as a Predictable Surgical Risk

IT IS rather generally believed that heart disease is less certainly an insurmountable contraindication to surgical operations than disease of the liver or kidneys. This has become increasingly true as the understanding and treatment of congestive failure has improved. Indeed, there seems to be a trend to reduce the preoperative evaluation of the heart to the recognition of congestive failure. Evidence for this opinion is the often repeated assertion that cardiac reserve is adequate when the patient can sleep lying down and walk up a flight of stairs without dyspnea or pain. This eminently practical approach to the problem of heart disease was one of the first postulates of Sir Thomas Lewis, but it should be remembered that it was designed to evaluate heart function during the course of usual living. Recently it has been recognized that there is an increasing incidence of sudden failure or arrest of the heart during surgical operations. For the most part, these catastrophes have occurred in individuals without prior evidence of diminished tolerance to exercise.

The recognition of impending sudden failure or arrest of the heart has become a pressing obligation. Special problems arise with two classes of patients: those with aortic stenosis and those with first degree heart block.

Aortic stenosis predisposes to sudden death during surgical procedures. The lesion precludes effective cardiac support of the peripheral circulation when blood volume is reduced by surgical blood loss. Furthermore, alarming hypotension and ineffective coronary circulation may result from the diminished peripheral resistance of general anesthesia or anoxia. The clinical recognition of aortic stenosis fortunately presents few difficulties.

First degree heart block can be recognized only by measurement of the P-R interval on an electrocardiographic record. It is an ominous finding because of the hazard of complete auriculoventricular dissociation and ventricular standstill during surgical or anesthetic stress. Digitalis, quinidine, and Novocain increase the likelihood of these complications. Ephedrine-like compounds offer considerable promise in the treatment of delayed conduction time, but their most effective utilization requires further study. It is not uncommon for patients to present coexisting first degree heart block, congestive failure, and severe anemia. Under such circumstances, careful digitalization with short-acting glucosides may be necessary to permit correction of the

anemia with concentrated red cells. Withdrawal of digitalis is often possible after anemia is corrected and is an indicated preoperative safeguard. It is also helpful to have established the response to Adrenalin before operation.

There remains for consideration a group of patients destined to develop cardiac arrhythmia during operation in spite of a normal exercise tolerance, no aortic stenosis, and no heart block. Prophylactic quinidine has fallen from favor because of undesirable side effects and because of a growing conviction that cardiac arrest in a quinidinized patient is especially refractory to restoration of cardiac rhythm by massage. The logical approach to this problem is the more careful scrutiny of cardiac function throughout the period of anesthetic and surgical stress. The cathode-ray oscillograph and the pulse tachometer have proved helpful to us for this purpose. It is surprising how frequently in elderly patients, during induction and intubation, there occurs a series of ventricular premature beats comparable to those seen regularly during manipulation of the mitral valve. Such evidence of cardiac irritability seems likely to have prognostic import, aside from its sobering influence on the anesthetist.

A further virtue in the constantly visualized electrocardiographic record is the sound basis for selection of drugs for specific arrhythmias: Cedilanid for supraventricular tachycardias, Novocain compounds for ventricular premature beats, and ephedrine compounds for prolonged conduction defects. Such precise therapy, with immediate observation of its effectiveness, has obvious advantages over blind therapy and renders questionable the use of a combination of Novocain and Adrenalin. The oscillograph not only provides immediate and certain evidence of cardiac arrest, but also defines impending and established ventricular fibrillation with great clarity.

It seems reasonable to conclude that evaluation of the cardiac risk during surgery should include, in addition to the exercise tolerance test, some consideration of the vulnerability of the heart to arrhythmia. It is suggested that a continuous electrocardiographic record during anesthetic induction may permit recognition of an irritable heart with postponement of the operation and more careful preparation. It also seems likely that early recognition and appropriate treatment of incipient irregularities may reduce the incidence of ultimate cardiac arrests.

—Champ Lyons

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

RIB FRACTURES FROM MUSCULAR EFFORT WITH PARTICULAR REFERENCE TO COUGH

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THE appearance of pleural pain following cough may be the result of fracture of one or more ribs. Although such fractures are not extremely common, they are certainly not rare, and the possibility of their occurence is especially to be considered in the presence of otherwise unexplained pleural pain. Some idea of the incidence of these fractures may be obtained from several investigators. In an interesting study of 500 patients with atypical pneumonia in an Army station hospital made by Harvey[72] in 1942-1943, 19 had recent rib fractures; excluding one with a history of trauma, there remained an incidence of 3.6 per cent. Many of these had been overlooked at the original examination. The serial studies made during the course of the pneumonia would often reveal a callus, and review of the earlier films showed fracture lines at the same site. In several cases reviewed, these fractures were quite apparent, but the attention of the examiner was centered on the more obvious inflammatory process in the lungs. In an analysis[116] of 1,194 incipient cases of tuberculosis, there was one patient with a rib fracture (0.08 per cent); among 601 moderately advanced cases, there were 12 patients with rib fractures (2 per cent); and among 108 far-advanced cases, there were 7 with rib fractures (6.5 per cent). Oechsli,[105] who routinely examined patients for rib fractures, found 22 (0.7 per cent) with such fractures in 3,000 admissions to Olive View Sanatorium. A careful search for fractures of the rib following cough among 64 patients with pleural pain in whom no other cause was apparent was made by Mitchell; of these, 14 (21.9 per cent) had fractured ribs.

HISTORY

The first instance of rib fracture produced by coughing that could be found in the literature is the one reported by Gooch[61] in 1773. His patient suffered from necrosis of a rib caused by a kick. When nearly recovered, he fractured a rib on the opposite side during a paroxysm of coughing. Monteggia[100] in 1802 reported seing a man of about 50 years of age who had fractured a rib while coughing. The sound produced at the moment of fracture was heard by all in the room.

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In 1834, R. J. Graves[63] of Dublin reported in excellent detail what he considered to be the first case of this nature.

> A 47 year old woman, tall and unusually strong and muscular for a female, had a violent fit of coughing 5 days previous during which she suddenly felt a stitch in the left side, with a sensation of something snapped or given way. The pain was so severe and so affected her breath she sought professional advice when some leeches and afterwards a blister were applied without relief. Inspiration was painful and pain radiated down to the left kidney and up to the right shoulder. The central point of tenderness was at the midpoint of the 9th or 10th rib and that from which the pain radiated was situated not between the ribs but on one of them. Pressure made at exactly this spot could scarcely be tolerated. She had observed that she was much easier during the days when her stays were on, than at night when she had unlaced and taken them off. A compress and roller over the part affected afforded immediate relief. Altogether the case is instructive not merely for its singularity, but because it affords a useful lesson with regard to the extreme importance of making an accurate examination of every disease before we hazard an opinion concerning its nature.

The following year at Val-de-Grace at the examination of a patient suffering from chronic pneumonia, Broussais[26] found a painless tumor, the size of a pigeon's egg, on the fourth rib; crepitus was elicited and a fracture was diagnosed.

In 1838, the scholarly and erudite surgeon Malgaigne[89] published a most impressive survey of the medieval and ancient medical literature on fractured ribs; he had been able to collect 7 cases. Early case reports were also published by Nankivell (1836),[103] Bérard (1841),[15] Hilton (1852),[74] Denonvillier (1853),[39] and Hérard (1855).[73]

In 1860, Gurlt[67] recorded 14 instances of rib fracture from muscular action; 10 of these were from coughing, 1 from a repressed sneeze, and 1 each from turning in bed, mounting a restless horse, and through an effort to maintain bodily equilibrium.

In 1882, Mazeillé[94] published a series of 24 cases including one previously unreported. In 1890, the list was extended by Tunis[132] to a total of 40 rib fractures from muscular action. In more recent times Wahl[134] (1926) collected 66 cases (including 3 personal cases). Oechsli[105] (1936) reported 22 personal cases and Mitchell[99] (1951), 14 personal instances.

ETIOLOGY

Rib fractures from muscular effort occur as the result of the most varied circumstances but especially following a violent paroxysm of coughing. The most frequently identified cause of the cough in the reported cases has been tuberculosis, but it is likely that the frequency of roentgenographic examination of tuberculous persons accounts for this apparent excess. Thus, Cohen[36] reported 7 such instances, Richardson[116] 30, Oechsli[105] 22, and Webb[135] 3. Richardson[116] stated that there were ten times as many such fractures in patients with advanced as in those with incipient tuberculosis. It is true that as the disease worsens the cough becomes of greater severity and frequency; prolonged bed rest predisposes to osteoporosis.

Mazeillé[94] considered bronchitis the chief cause of rib fractures; certainly a large number of isolated instances have been ascribed to acute or chronic bronchitis, influenza, coryza, infections of the upper respiratory tract, and the like. Bronchial asthma is not infrequently mentioned. Laryngeal irritation from aspirated foreign matter has been the cause of rib fractures in 2 or 3 reported cases. In one young woman, both eleventh ribs were fractured during a paroxysm of whooping cough.

Sneezing has been blamed for the broken rib in several reports in the literature. One concerned the patient of Castella[31] (1861), a powerful 39-year-old Swiss hotelkeeper. Although he did not use snuff, on one occasion he took a pinch of it from a guest. After sneezing repeatedly, he attempted unsuccessfully to suppress the act by expanding his thorax with his mouth closed. A powerful exhalation followed, after which there was a definite crack accompanied by pain and difficulty in breathing. In explaining his case, Wyman[138] (1885) remarked that in the act of sneezing two powerful sets of muscles may be brought into antagonism in such a way as to expend their opposed forces on the ribs, making the fracture simply a mechanical matter. Podrazki[112] reported the case of a strong healthy lady "of some thirty years" who fractured the tenth costal cartilage while sneezing.

It is well known that coughing often follows vigorous laughter. Speed[126] and Palfrey[106] as well as Breslin[23] have called attention to rib fracture under such circumstances. Muscle strain incident to straining at stool or vomiting has also resulted in this accident.

Bones have been broken as a result of intervention of muscles not primarily concerned with respiration; these may act alone or in conjunction with those involved in such physiologic acts as are discussed in the preceding paragraphs. Thus, the patient of Atkinson[10] fractured a rib after coughing while in the act of hanging up his coat; Somerset[124] reported the case of a patient who fractured a rib after coughing while removing her stays; in Seilin's[121] report, the rib fracture followed cough while the patient was attempting to close a window. The patient of Fisk[54] after a sudden violent cough felt a rib break while sitting sidewise on a chair, with his legs crossed, his right arm and his hands clasped on the back of the chair. Groninger's[64] patient made an effort to right himself to prevent falling while walking home, with immediate pain and dyspnea resulting. Aitken and Lincoln[4] reported the instance of a well-developed and -nourished white man aged 29 years who with a cardboard box on his head was climbing a ladder; the box slipped, and to maintain balance he jerked his head suddenly to the right, thereby fracturing the left first rib. Analogous perhaps are those accidents induced by suddenly turning in bed or attempting to mount a restless horse. Rectification of asymmetrical posture seemed operative in the instance of Michael-Phillip's[97] young woman who had been out earlier with her young man. On arising from the bank on which they had been sitting, she felt something snap "like a twig"; a rib fracture was demonstrated roentgenographically.

A frequent complaint of occasional golfers is soreness or tenderness over the lower left ribs and upper abdomen. These might well be symptoms of fractured ribs. Two medical colleagues fractured ribs on the golf links, and a similar accident was at first thought to be due to coronary artery disease (Case 2). Fractured ribs are also said to be common among scullers; Arnold[9] reported a broken rib from a medicine ball workout, and Mandl[91] one from the Telemarkschwung in skiing.

When one is set to perform some action requiring heightened muscular activity which does not eventuate, rib fractures may occur. Chenery's[34] old but active farmer broke three ribs when a root which he was pulling up gave way, causing him to sit suddenly on a rock behind him. Kevin Byrne[28] described a case in which muscular effort alone accounted for six badly fractured ribs, three on each side. His patient was tossing cabbages with a pitchfork, and a particularly heavy forkful slipped off as he started to toss; the anticipated exertion was used on the lightened load. Perhaps the case of Nancrede[102] is parallel. The patient was a healthy vigorous laborer who fractured the second rib while trying to straighten a scythe blade; he was holding it down with one hand while lifting the free end with a monkey wrench held in the other hand when the accident took place.

SEX

There is no doubt that in instances in which these fractures are due to violent muscular action other that that involved in coughing or sneezing, men are definitely more prone to these injuries. Also, men are more often exposed to physical trauma, and fractures of all sorts from external violence predominate in men. This is not the case when the responsible forces derive from physiologic or quasiphysiologic activities (coughing, sneezing, vomiting, straining at stool, parturition). In 140 such instances in which the sex was noted, there were 85 women and only 55 men.

AGE

On a priori grounds, it might be anticipated that increasing age would incline to a heightened incidence of rib fractures. In addition to their greater dependence and helplessness, as a rule there is in aged individuals progressive atrophy of bones resulting from senile osteoporosis. Increasing calcification of the costal cartilages and the tendency to ankylotic fusion of the ribs with the vertebral column lead to reduced elasticity of the thoracic cage. Moreover, the wasting with senescence of muscles which formerly protected the ribs exposes them especially to indirect as well as to direct violence. The fact seems to be, however, that this very decrease in muscularity precludes the development of stresses adequate to break the now more predisposed ribs.

On the other hand, in youthful individuals the elasticity of the ribs affords a significant measure of protection. In quite young people, rib fractures from muscular action alone must be extraordinarily rare. One exception must be made. Cough develops in patients with progressive rickets, and this

cough may occur in paroxysms. In a study of 32 children, ranging in age from 8 months to 4½ years, who suffered from severe rickets, Park and Howland[109] found rib fractures almost regularly present. In one case, 20 were counted. Although these fractures were often not apparent on physical examination, the roentgenograms of the patients studied by Park and Howland characteristically showed remarkably slender porous-appearing ribs. Pospischill[114] described a "dozen" instances of fractured ribs in autopsies of children who died from whooping cough; perhaps they also had rickets. In the 113 reported cases in which the age was specified, the youngest was a 16-year-old girl; 3 were 18-year-old and two 19-year-old women. The majority of the remainder occurred in patients in the third to sixth decade. Thus, the likelihood of rib fracture from muscular action is greatest from 20 to 50 years of life, that is, when the resiliency of extreme youth is lost but the feebleness of advanced years is not yet apparent (Table I).

TABLE I. DISTRIBUTION OF RIB FRACTURES BY AGE AND SEX

	AGE (YEARS)							TOTAL
	10-19	20-29	30-39	40-49	50-59	60-69	70-79	
Men	2	5	8	12	6	4	4	41
Women	6	18	16	14	10	6	2	72
Totals	8	23	24	26	16	10	6	113

PREGNANCY

In the literature there are reports of 24 rib fractures during pregnancy, all of which occurred in the last trimester, but only two during labor. Ahern's (1894)[3] patient, a strong, healthy woman in labor with her third child, sustained a fracture of the left sixth rib a little in front of the anterior axillary line when she was seized with a violent fit of coughing during a severe pain accompanied by powerful expulsive efforts. Freeland's (1895)[57] case, which seems to have escaped general attention, is quoted because of its interesting features: "A black woman of Herculean frame, who in a long pain during parturition fractured the eighth and ninth ribs on the left side. I was present when the accident occurred, and the loud report I heard when the bones gave away proves, I think, that although the ribs were large, solid, and fixed they were not strong enough to resist the powerful action that was being exerted by this unusually muscular woman."

Reference to Table II will show, as noted by Paulley and co-workers,[111] that in these cases the fractures occur late in pregnancy, tend to be left-sided, and affect chiefly the lower ribs. Paulley and co-workers also pointed out that multiple fractures are exceptional under such circumstances, but this observation is not confirmed in the present series.

Cazeau[32] asserted that there is an increase of fragility of the ribs in pregnancy because of fetal demands on maternal calcium. This idea has been alluded to repeatedly by later writers on the subject, but it was first studied critically by Paulley and co-workers. Their comparisons of bone density with controls of the same sex and age revealed slight osteoporosis in only one case; blood calcium and phosphorus estimations were within normal

limits. Barr (1949)[13] is of the opinion that some degree of decalcification may be present late in pregnancy although it is not revealed by roentgenographic or blood chemistry studies. Lachmann and Whelan[82] experimentally removed calcium by acid and studied roentgenographically the bones before and afterward. It is clear from their results that normal roentgenograms do not exclude osteoporosis, for only under favorable circumstances can decalcification of less than 20 per cent be diagnosed roentgenologically. In most bones, including the ribs, the calcium loss, in order to be visible, must be in the vicinity of 20 to 40 per cent.

TABLE II. SUMMARY OF REPORTED RIB FRACTURES DURING PREGNANCY

SOURCE	AGE (YR.) AND PARITY	DURATION OF PREGNANCY	SITE OF FRACTURE (RIB)	EXCITING CAUSE
Adkins (1949)	36	1 week before confinement	Left 7th and 8th	Cough
Ahern (1894)	Multipara	In labor	Left 6th	Coughing paroxysm
Barr (1949)	26	36 weeks	Left 11th	Coughed while rising from bed
Benoît		9th month	Left 9th	Coughing fit from chronic bronchitis
Blanc (1908)	37	End of pregnancy	Multiple	Cough
Brookhouse (1879)	36	Late pregnancy	Left 6th	Coughed while sitting sideways
Chenery (1878)	23			Coughing fit
Dogadkin (1885)	27; multipara	10th month	Left 8th	Bronchitis
Evans (1949)	Late 20's; multipara	8th month	Left 8th and 9th	
Freeland (1895)		In labor	Left 8th and 9th	Straining with hard pain
Hérard (1855)	22	7th month	Mid ⅓ of left 11th	Violent cough from chronic bronchitis
Inglima (1938)	29	Last of pregnancy	Left 9th	Coughing fit (acute bronchitis)
Miall (1871)	29	7th month	10th	Violent paroxysm of coughing
Paulley, Lees, and Pearson (1949)	21; primipara	36 weeks	Left 10th	Coughing fit (chronic bronchitis)
	25; multipara	38 weeks	Left 9th and 10th	Coughing mildly
	36; multipara	40 weeks	Left 11th	Lifting and coughing
	25; multipara	29 weeks	Left 11th	Coughing after previous choking
Telhouni (1937)	40; multipara	8 months	Left 11th	Asthmatic attack
Trillat and Pizzera (1932)	34; primipara	8 months	Left 10th	
	27; multipara	8 months	Right 11th and 12th	Bronchitis
	32; multipara	4 days before delivery	Right 11th and left 7th	Bronchitis
	35; primipara		Left 11th	
Vidal (1894)	32; multipara	7th month	Left 10th	Bronchitis
Wynn-Williams (1951)	28	6 months	Right 6th	Coughing from respiratory tract infection

In any case, gestation does not retard consolidation in spite of the classic conception to the contrary; in the case reports in which comment was made, healing was noted to progress normally even before delivery.

The presence or absence of increased fragility of bones in late pregnancy would in no way explain the left-sided preponderance of these frac-

tures. It has been suggested that the position of the liver seems to protect the right ribs, the net effect of the blow being delivered against the lower left ribs. Paulley and co-workers considered that the laterality was favored by the bulky uterus being driven violently upward and backward with forceful contractions of the abdominal muscles in coughing or sneezing. They further called attention to the posteral alterations in the pregnant state: compensatory to the backward thrust of the head and shoulders is a lordosis with increased tone of the sacrospinalis. In their view, incoordinate action in association with depression of the lower ribs by the iliocostalis could provide conditions for a shearing stress sufficient to fracture a lower rib. Telhouni[128] commented on the exaggerated distension of the abdomen in advanced pregnancy and on the derangements provoked thereby in the last ribs; thus the direction of forces generally applied by the ribs is modified, at times deleteriously. None of these speculations is satisfactory, and it may well be that the explanation can be found in a combination of these with as yet unappreciated factors.

SITE AND NUMBER OF THE FRACTURES

Fractures resulting from cough have been reported in every rib, but rarely occur in the uppermost and lowermost ribs. The first rib is, however, frequently the site of fracture from muscle stress unrelated to cough. Most fractures are found in the fifth through the tenth ribs (Table III). As a rule (102 of 142 instances), a single rib is involved. In 15 patients, two ribs were broken; in 12 patients, three ribs; four and six were broken in four instances each; and eight were broken in one person. There are a number of reports in which it is clear that in multiple rib fractures not all of the ribs break simultaneously. Edgecombe's[49] patient sustained a fracture on the left side; one week later a second break took place on the right. The second fracture in Halliwell's[68] case occurred sixteen days after the first. Evans'[51] patient felt the second rib crack with a subsequent bout of coughing about twenty minutes after the first. In the case reported by Swineford and McKinnon[127] there were eight independent rib fractures during one single bout of upper respiratory tract infection.

TABLE III. DISTRIBUTION OF RIB FRACTURES BY SITE INVOLVED

LOCATION	RIB												TOTALS
	1	2	3	4	5	6	7	8	9	10	11	12	
Right side	0	0	1	2	9	15	19	10	9	4	5	1	75
Left side	1	1	0	2	7	21	18	16	14	8	6	0	94
Totals	1	1	1	4	16	36	37	26	23	12	11	1	169

Analysis of the location of fractures in the cases reported in the literature suggests that those in the first rib seem conditioned by the attachment of the scalene muscles as well as by the subclavian groove. There were too few fractures in the second, third, and fourth ribs to elaborate on this point. There was a definite increase in incidence of fractures between the anterior and posterior axillary lines from the fifth through the ninth ribs.

They were less commonly found mesiad to this area and were definitely rare adjacent to the cartilages and vertebral column.

Reference to Table III shows that in those instances in which the side involved was noted, there was a moderate preference for the left. In the 134 case reports in which this point was recorded, 7 patients had bilateral fractures, the remainder (approximately 93 per cent) having but one side involved. The discrepancies in the various totals stem from the lack of detail in many instances.

PSYCHOSOMATIC FACTORS

The old-fashioned fault of carelessness and its counterpart carefulness have been replaced in more modern circles by accident proneness and compulsive behavior. Much has been written on accident proneness as a cause of fractures.[30, 45, 46] Only one reference was found to emotional or psychosomatic factors in the reported cases of rib fracture. In a letter to the editor of the *British Medical Journal,* Harold[70] wrote: "A young female, after some months estrangement from her boy friend met him again, was lovingly embraced, and soon after experienced what she described as a sharp pleuritic pain in the chest. Medical opinion was nonplussed for three days when an x-ray revealed a fractured lower rib. Could this, sir, be etiologically ascribed to emotional trauma?"

THEORIES

It is generally agreed that muscular contraction can fracture healthy ribs, but there is no unanimity either as to the precise muscles involved or to their method of action. In general, it is supposed that the accident takes place by virtue of opposed forces. Seilin[121] invoked the simultaneous contraction of the diaphragm and the upward pull of the latissimus dorsi. Tunis also believed that the diaphragm was a major factor, together with the other powerful muscles attached to the ribs. Oechsli,[105] whose views are most widely accepted, excluded the diaphragm from consideration because the attachments of this muscle do not correspond to the location of the fractures. In his cases, these fractures were found in a line extending from a point 4 cm. from the costochondral articulation of the fourth rib obliquely caudad and laterally to the ninth rib in midaxillary line. This line, he stated, corresponds to the interdigitations of the external oblique and the serratus anterior. The contrasting contractions of these muscles, in his view, produce the fractures.

Malgaigne[89] invoked torque: "in powerful inspiration preceding cough, slight torsion which the elevation of the sternum produces on ribs is not completely executed because of ossification of cartilages; bones are ruptured because they cannot yield." Telhouni[128] also favored the concept of torsion. Parenti[108] thought that the site of the fractures was conditioned by the moment of curvature which is greatest posteriorly near the region of the angle, and anteriorly near the costochondral junction.

Sustained tetanic contractions are quite capable of breaking bones; such fractures may appear in 35 per cent of patients subjected to electric shock

therapy,[95] or in 23 per cent of those treated with Metrazol.[47] Fractures have also been reported in tetanus: in the ribs and vertebral column,[84, 117] elbow,[125] femoral neck,[12] and forearm.[137]

Moreover, it is by now well established that repeated subminimal trauma may produce fracture, particularly of weight-bearing bones. Large numbers of such fractures have been reported under various names (March fracture, March foot, Deutschländer's disease, Pied forcé, fracture de recrue) ever since World War I, although they were known earlier.[22] This mechanism has been called on to explain rib fracture from coughing, a view which has been championed especially by Zur.[140] He doubts that such fractures come about from a particularly strong cough, feeling it more likely that they are instances of "schleichende Frakturen" (creeping fractures). Alderson,[6] too, considered stress from repeated contraction of the scalenes to be a plausible explanation of breaks of the first rib appearing after strenuous physical training. The constant location of the fracture line in relation to the insertion of the scalene muscle is invoked as the explanation of rib fractures following thoracoplasty in the report of Guggenheim and Cohn.[65] They analyzed 208 cases of thoracoplasty in which fractures of the first or second rib or both occurred on the contralateral side in eight patients. After operation, the pull of the muscles on the first and second ribs is unopposed by similar muscles on the side operated on. The fractures did not take place during or immediately after the operation. The authors commented that it was noteworthy that all fractures with one exception occurred in the area of greatest muscular stress and where the bone structure was thinnest due to the subclavian grooves. Further reference to these points is made in the structural analysis section.

STRUCTURAL ANALYSIS OF RIB FRACTURES FROM MUSCULAR CONTRACTION

Before the structural analysis is discussed, it is considered best to define, from an engineering standpoint, those terms which may be used differently in other fields. When a force is applied to an object, the object is subjected to *stress;* the fundamental stresses may act singly or in combination. The diagrams in Fig. 1 illustrate these stresses, which are called *tension, compression* (direct stresses), *shear,* and *bending.* As a result of these stresses the object undergoes *deformation;* this deformation is called *strain. Enlongation* is the strain which results from tensile stresses; under compression the body is shortened; as a result of shearing stress, one part of the body tends to slide past the other. When one prunes a branch in his garden, he is subjecting the branch to a shearing stress.

In order to facilitate and simplify the engineering analysis, an object is isolated from its surroundings by means of a *free body diagram* which permits the application of vectors to those points at which forces are acting. This principle is shown in Fig. 2.

A moment, mathematically defined, is $\int(x\text{-}a)^k dm$, where dm is the differential of measure over the appropriate portion of space. In engineering

it is customary for k to be 1 or 2, that is, for the first and second moments only to be used. The first moment is the moment of a force; the second is the moment of inertia.

The *moment of a force* ("moment") with respect to a point is the tendency of the force to turn or rotate about the given point. This tendency to rotate is expressed as the force times the perpendicular distance from the line of action of the force, as illustrated in Fig. 3. In this analysis, three basic

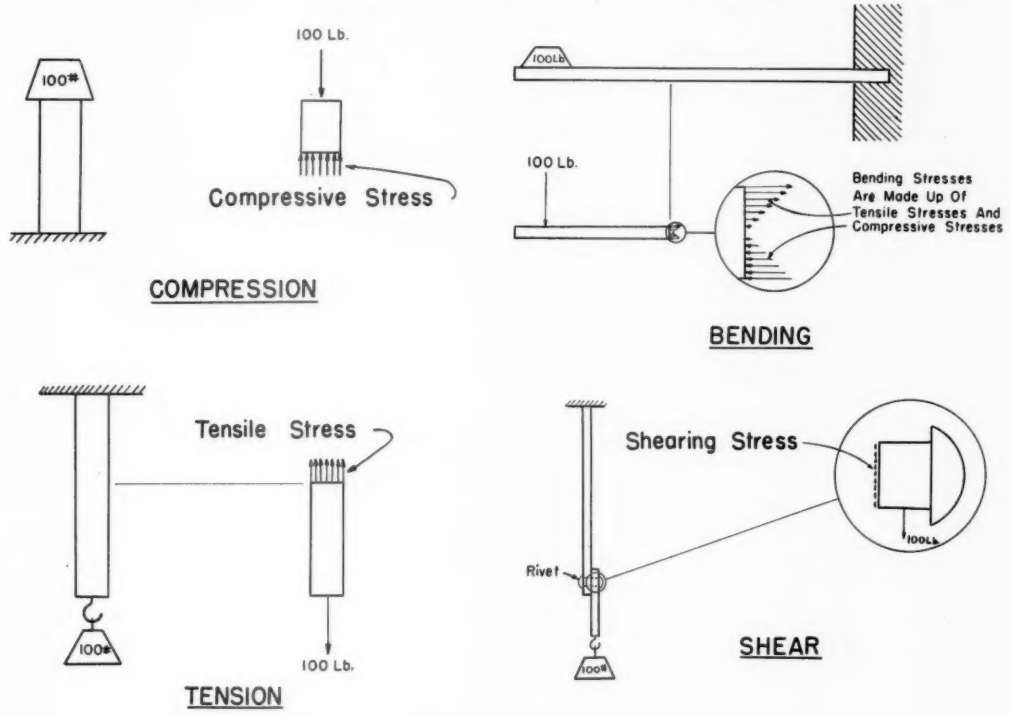

Fig. 1.—The fundamental stresses.

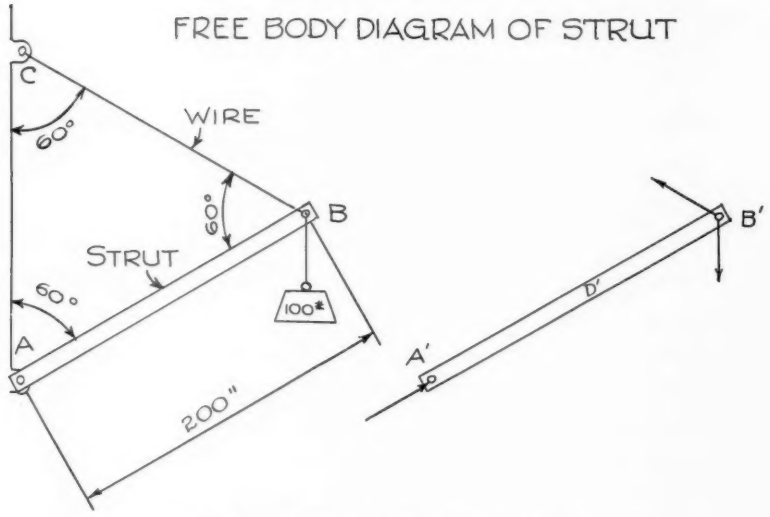

Fig. 2.—Free body diagram of strut.

laws of static equilibrium have been used: (1) summation of horizontal forces acting on a free body equals zero, $\Sigma F_x = 0$; (2) summation of vertical forces acting on a free body equals zero, $\Sigma F_y = 0$; (3) summation of moments of forces acting on a free body about any point in the free body equals zero, $\Sigma M = 0$. In the free body diagram of the strut, which represents a condition of static equilibrium, these principles can be applied to solve for the unknown forces acting on the body as shown in Fig. 4.

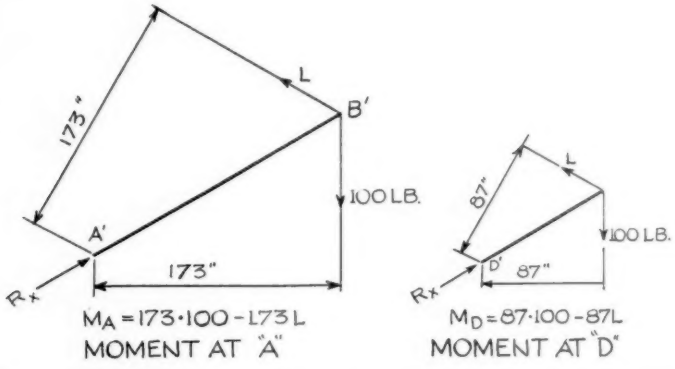

Fig. 3.—Example of computations of moment of a force with respect to points "*A*" and "*D*."

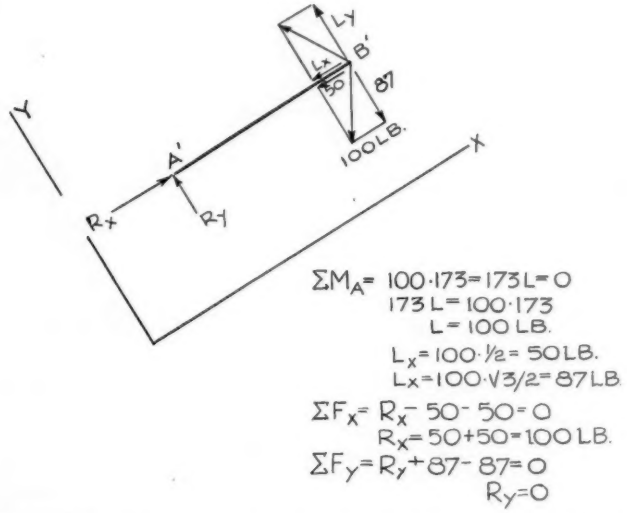

Fig. 4.—Computation of unknown forces. R_X and R_Y are reactions with respect to the x and y axes; L_X and L_Y are components of L with respect to the x and y axes; F_X and F_Y are the resultant forces on the x and y axes.

Of the reported rib fractures from muscular action, the sixth rib was involved the greatest number of times and, therefore, this one was selected for the structural analysis. The first step was to draw a free body diagram of this rib and solve for the reactions. (See Fig. 5.) *Reactions* in this sense are resultant forces at the supports of the ribs, that is, the costochondral junction and vertebral column due to muscular action. At various points along the rib, imaginary cross sections were established and stresses were computed at

these points. These stresses consisted of shearing stresses, tensile stresses, compressive stresses, and bending stresses. For example, in order to compute the stress in Section 4, a free body diagram was established for the portion of the rib extending from the vertebral column to Section 4. The free body diagram and computations of stresses at Section 4 are shown in Fig. 6. Bending stress was computed from the formula $f = \frac{M}{S}$ in which S is the *section modulus,* M the moment at the section, and f the extreme bending stress. The section modulus is the *moment of inertia* divided by ½d. For

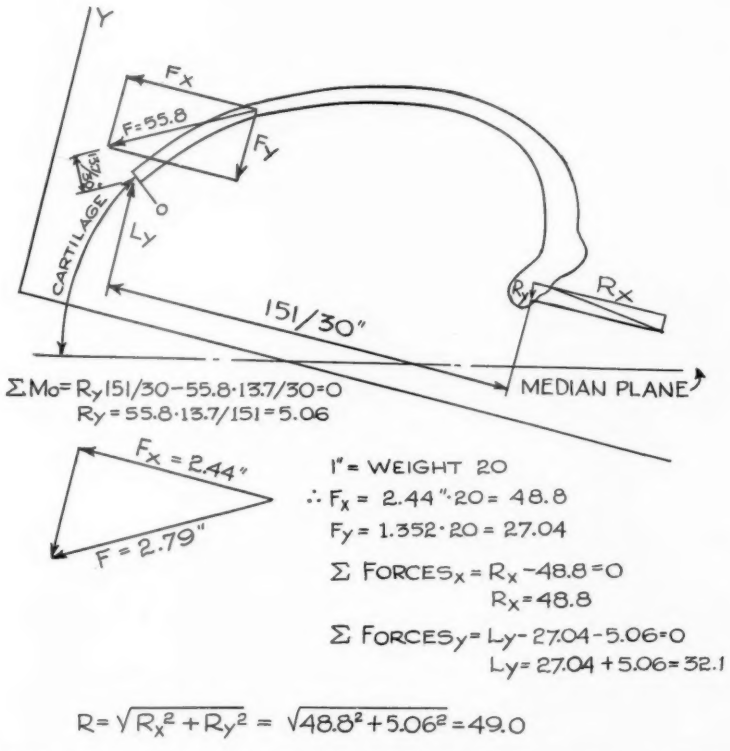

Fig. 5—Free body diagram of sixth rib with calculations of reactions at costochondral and costovertebral junctions.

the purposes of calculating stresses, the rib sections were assumed to possess properties of equivalent ellipses. Table IV summarizes the values obtained from computations at the various sections indicated. It should be noted that direct stresses and bending stresses at the same section are additive. In Fig. 7 is shown the variation of the combined direct and bending stresses along the rib. The variation of shear stresses is shown in Fig. 8. In each case the relative magnitude of the stresses at the various sections is represented by the distance from the center line of the rib to the curve. Sites of reported fractures are indicated on the ribs themselves. The incidence of fractures in each zone is indicated by encircled numbers. Fractures are

of greatest frequency in those areas where bending stress is greatest; they are of least frequency where shearing stress is maximal. Torsion is not believed to be present, but if there were any torsion present it would be in the portion

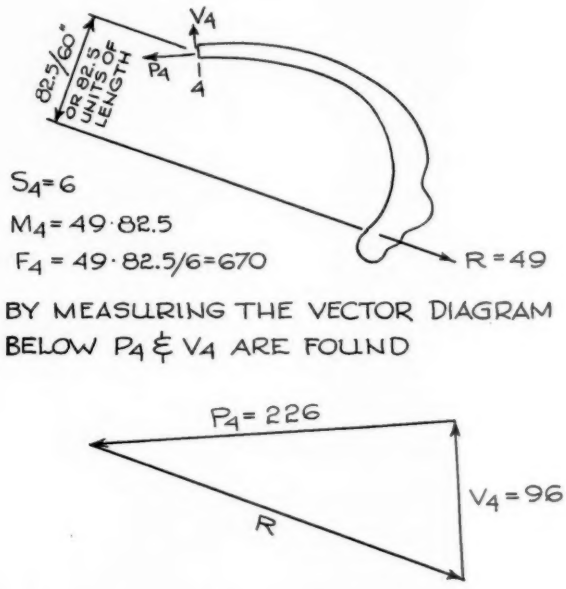

Fig. 6.—Free body diagram with computations of stresses at Section 4.

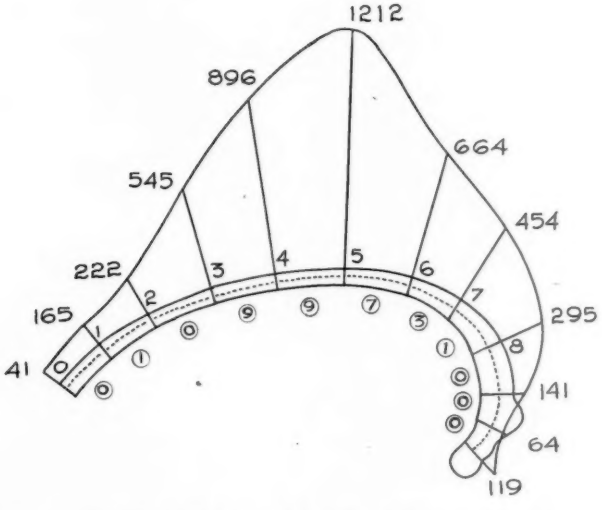

Fig. 7.—Variation of combined direct and bending stresses along the rib. See text.

of the rib extending from Section 7 posteriorly; fracture produced by torsion in this portion would tend to assume a helical path.

The actual fracture may be the result of a gradual failure of the rib due to a progressive cracking across a given section. Even though the stress at this section may be computed to be below the *elastic limit,* stress concentrations

in minute regions occasionally exceed the elastic limit. The elastic limit is the maximum stress to which a material can be subjected without any permanent deformation. Prior to the development of a crack, there is a period of inelastic deformation which is graphically illustrated in Fig. 9. Cracks are

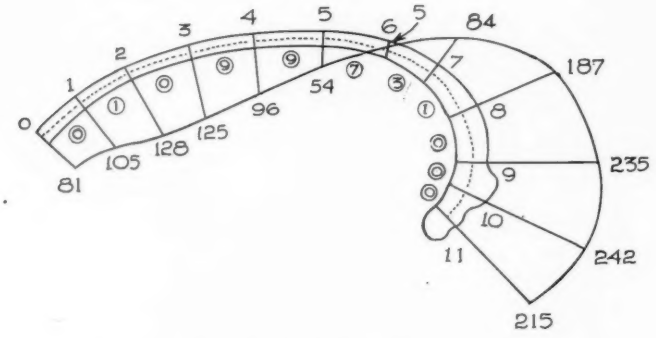

Fig. 8.—Variation of shear stresses. See text.

thus started which reduce the cross-sectional area resulting in an increase in maximum stress, as illustrated in Fig. 10. This cycle is repeated with progressive reduction in area of intact bone, which may suddenly snap. Throughout the failure, the region of high stress has always been so small that the deformation does not extend sufficiently to become apparent. This mechanism is illustrated by those patients in whom a definite localized area of tenderness persists for several days prior to audible fracture at this site.

TABLE IV. VALUES OBTAINED FROM STRESS COMPUTATIONS AT DESIGNATED SECTIONS OF SIXTH RIB

SECTION	S*	y*	M*	f*	P*	A*	p*	f + p*	V*	v*
0	18	0	0	0	141	1	141	141	81	81
1	18	22.5	735	40.9	124	1	124	165	105	105
2	14	52.5	1710	122	100	1	100	222	128	128
3	9	61.5	3000	333	212	1	212	545	125	125
4	6	82.5	4020	670	226	1	226	896	96	96
5	5	98.6	4860	972	240	1	240	1212	54	54
6	12	103.0	5030	419	245	1	245	664	5	5
7	21	96.5	4710	224	230	1	230	454	84	84
8	27	76.0	3710	137	158	1	158	295	187	187
9	30	44.0	2150	72	69	1	69	141	235	235
10	30	20.5	1000	33.3	31	1	31	64	242	242
11	30	0	0	0	119	1	119	119	215	215

*Symbol notation:
S = Section modulus,
y = Perpendicular distance from center of section to the line of action of the reaction at support,
M = Bending moment at section,
f = Maximum bending stress at section,
P = Direct force on section,
p = Direct stress on section (p = P/A),
A = Cross-sectional area of rib, which is taken as 1 since it is practically constant at all sections,
V = Shearing force on section,
v = Shearing stress on section.

In the foregoing analysis, certain assumptions were made initially.

1. The weight of the rib was assumed to be negligible. This would not have altered the location of the maximum stress.
2. The support of the rib at the vertebral column was assumed to act as a hinge joint.

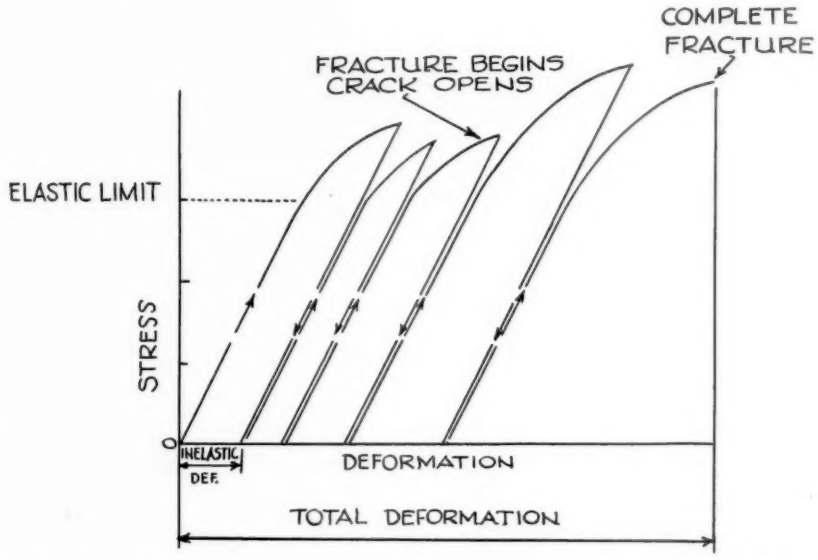

Fig. 9.—Stress-strain diagram. In coughing, the rib returns to its initial dimensions, the zero position, as long as the elastic limit is not exceeded. When the elastic limit is exceeded, it no longer returns to the zero position but a certain small amount of permanent set takes place which is indicated by *inelastic deformation*. Each time the elastic limit is exceeded, the inelastic deformation is increased. Ultimately the rib breaks.

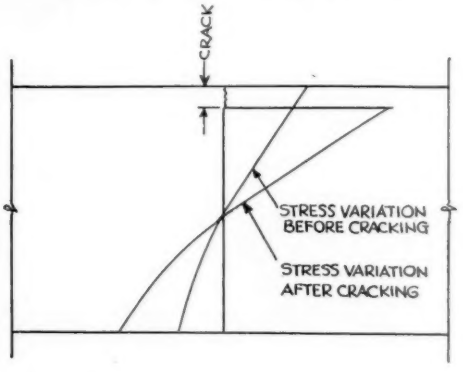

Fig. 10.—Example of change in stress variation caused by small crack in rib. The parallel horizontal lines represent the upper and lower margins of the much enlarged rib. It will be seen that prior to the crack the displacement of the stress line from the vertical is considerably less than after the cracking has begun. As the depth of the crack increases, the maximum stress in the remaining intact bone is progressively increased. Finally, complete fracture results.

3. The anterior support was taken to be at the costochondral junction; the moment induced by the cartilage was considered to be negligible.
4. It was assumed that the rib was supported only at its extremities.
5. It was assumed that there was no chance of failure in a vertical plane because of the uniform action of the intercostals and also because of the ratio of the depth of the vertical plane to the depth of the horizontal plane of the rib. Strength varies directly with the cube of the depth.

6. It was assumed that the section modulus was proportional to the outside dimension of the rib, that is, that the ratio of the cross-sectional areas of the compact bone to the cross-sectional areas of the cancellous bone did not vary and that the cancellous bone trabeculae were uniformly distributed. Consequently, stress units are of arbitrary dimension.
7. It was considered that muscle force is directly proportional to its effective cross section,[50] and that in addition the Muskelkrafteinheit of Fick[53] (10 kg. per square centimeter) is valid in so far as it permits contractile forces of various muscles to be compared. This force has been estimated by Franke[55] to be 11 kg. per square centimeter.
8. It is clear that a number of variables are also involved in the area of cross section of the respiratory muscles, variations not alone from age, sex, and muscularity of the individual, but also from the effect of the incident disease. As a standard, the *Cross-Section Anatomy* of Eycleshymer and Shoemaker[52] was employed.
9. A mean position of the rib was assumed. A series of roentgenograms was taken on full inspiration and expiration in the hope of deriving information useful to this analysis. Extent of thoracic expansion and degree of costal or diaphragmatic breathing varied not only from person to person but also in the same person at different times.
10. Other stresses, such as radial stresses, have not been discussed, as they are negligible.
11. Bending stresses were assumed to vary along a straight line instead of hyperbolically as they actually vary. It is realized that this assumption yields inaccurate stress calculations, but since the ratios of the radii of curvature to their corresponding depths are not of great magnitude, the variation of maximum stresses along the rib would be similar to that obtained by virtue of this assumption.

The criticism might be offered that an analysis based on so many assumptions could not produce valid results. Rashevsky[115] pointed out that the study of such nonreal idealized systems does lead to practical results, at least within certain limits; within these limits the real things have common properties with the fictitious idealized ones. "Only a superman could at once grasp mathematically all the complexities of a real thing. We ordinary mortals must be more modest and approach reality asymptotically, by gradual approximation."[115] Finally, there is a close correspondence of the predicted and actual zones of greatest likelihood of fracture.

THEORY OF RIB FRACTURES DUE TO VIBRATION

Whereas many rib fractures are probably the result of stress concentrations and progressive cracking, as has already been explained, some fractures may be caused by a sudden muscular contraction that is repeated at a frequency which corresponds to the natural frequency of vibration of the rib. Under such a condition, the stresses and strains are tremendously increased. This can best be seen by inspecting the equation of motion of a spring under forced vibration,

$$\frac{W}{g}\frac{d^2x}{dt^2} = W - (W + kx) + P \sin t,$$

together with the magnification factor curve in Fig. 11. W is the weight acting on a spring, g is the acceleration of gravity, k is a physical property of

the spring called the spring constant, x is the deflection of the spring at time t, and the term P sin t is known as the disturbing force and is related to the magnification factor.*

Of course, the preceding equation pertaining to a spring is not directly applicable to the action of ribs, but the magnification curve for rib vibrations would take a similar form, and even though the vibration of a rib would be subjected to some damping, due to contiguous tissues, stresses and strains in excess of the elastic limit (and sometimes in excess of the ultimate strength) would be reached. This is due to the fact that the magnification factor approaches a limit of infinity at $\omega/p = 1.0$.

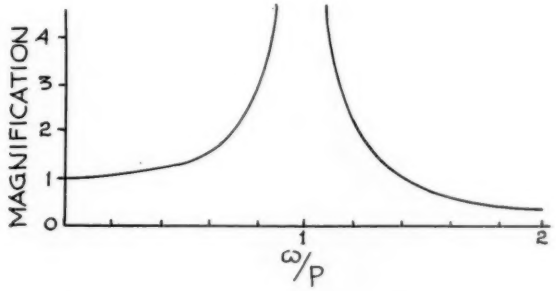

Fig. 11.—Magnification of forces results when coughing occurs at the natural frequency of vibration of the rib. At the time when $\omega/p = 1$, the force approaches infinity.

It should be pointed out that the probability of rib vibrations occurring at the natural frequency of a rib is extremely low; however, such a condition must have occurred, when one considers the periodic function of a coughing seizure and the billions of people who have had many coughs during their lifetimes.

PATHOLOGY

In those instances in which fractures produced by muscular action have been examined pathologically, essentially normal features have been revealed grossly and histologically. Hérard[73] reported a case of fracture of the eleventh rib on the left side which at autopsy showed rich callus at the fracture site; the tissues of this rib and of the other bones as well were normal. Matthes and Thelen[93] excised two such fractures which were initially thought to be malignancies; biopsy showed new formation of bone and cartilage and no tumor but "reactive changes in the sense of callus formation." In the third case of this paper, the biopsied fracture disclosed essentially normal rib including bone marrow. Finally, Bodenheimer's[19] case showed little beyond osteoid formation with low-grade perichondritis.

It may be relevant to cite here the results of post-mortem examinations of vertebrae fractured during convulsions of tetanus. Eberstadt's[48] patient was a 29-year-old soldier. The autopsy disclosed in the third and fourth thoracic vertebral bodies numerous shattered, broken, and collapsed bone trabecu-

*For a complete explanation of this equation and graph see S. Timoshenko's Vibration Problems in Engineering, Chapter 1, D. Van Nostrand Company, Inc.

lae, which comprised a rather disordered group. In many places, the medullary cavity was replaced by an edematous vascular fibrillar marrow, which contained some plasma cells and round cells with much protoplasm. There was limited new bone formation with irregular calcification. There was no evidence of pre-existing bone disease.

Autopsy of a powerful boy, 15 years of age, in whom tetanus developed following a foot injury showed the fifth thoracic vertebra to be compressed and to project into the spinal canal. The fourth intervertebral disc was infiltrated with blood. Aside from the mechanical disorder, microscopic examination revealed completely intact bone.[11]

CLINICAL PICTURE

The symptomatology of rib fractures produced by muscular action does not differ from that produced by trauma. At the moment of the accident, many patients have felt something break or give way in the side; certain of these fractures have been accompanied by noises which at times could be heard across the room.[3, 7, 8, 38, 40] The noise is generally likened to that produced by breaking a stick, fagot, or twig. Pain is not an invariable symptom, especially in breaks of the uppermost ribs; thus, of Alderson's[6] 35 patients with fracture of the first rib, only 5 volunteered significant symptoms or history. The patient of Brewster[24] felt something snap in the chest but experienced no pain; three days later a small tender swelling was noted at the fracture site. The onset of pain may be sudden; 3 of Wynn-Williams'[139] 9 patients and 5 of Mitchell's[99] 14 reported development of abrupt pain. Patients stated, for example, that for days they had had aches in the side which suddenly became stabbing pains. Once present, the pain is usually intense and sticking or cutting in nature. All movements of the thorax, especially coughing, sneezing, or deep breathing, intensify the pain. Movement of the arm of the affected side, contracting the serratus magnus, or moving the trunk may similarly worsen the discomfort. The pain is accompanied by an instinctive restriction of respiratory motion and often by a splinting of the ipsilateral muscles of the thorax, particularly in instances of multiple fracture. If coughing continues, the pain will ordinarily interfere greatly with sleep. Severe pain persists from two days to two weeks. Some degree of discomfort probably persists for about three months. In a number of the reported cases, pain was present after six months. Just as with traumatic fractures, immobilization affords relief; Graves'[63] patient felt better in her stays and Mitchell's[99] patient was more comfortable when lying with the painful place pressed against a hard pillow.

The pain usually is localized in the area contiguous to the fracture site, but not infrequently it is referred along the distribution of the involved intercostal nerve. Particularly in fractures of the lower ribs, pain may extend to the hypochondrium, mediated through the anterior cutaneous branches of the sixth through the eleventh intercostal nerves. Pain may extend above as well as below the fracture site because of the superior and inferior branches of these nerves. Two instances of paradoxical referred pain have been re-

ported. Ginsburg's[60] patient complained of an aching pain in the right side of the neck; roentgenogram showed a recent fracture of the left first rib. Because the pain was on the wrong side, another roentgenogram was made and it confirmed the fracture site. Webb's[135] patient felt no pain at the termination of the ninth intercostal over the abdomen on the same side as the fracture, but had severe pain on the opposite side in this area of distribution.

Moderate to exquisite tenderness may be elicited by finger point pressure over the fracture site. Pressure on the rib at some distance from the site of injury causes pain in patients with rib fracture but not in those with contusions or muscular injury.

Innumerable instances of crepitus, at times audible at a considerable distance, are reported after rib fractures produced by coughing. Crepitation naturally is to be expected only in complete fracture; it is ordinarily not elicited in infractions or in insignificant separation of the fragments from one another. When present it is usually quite clear and may be felt with the palpating hand during ordinary respiration or heard with the ear or stethoscope applied to the chest. It is often apparent to the patient.[38, 104, 135] Gurlt[67] noted that crepitation could at times be elicited by applying pressure with the fingers of both hands placed on either side of the suspected fracture site. In order to appreciate the sound with the stethoscope or feel it with the applied palm, pressure might be exerted on the rib at a greater distance or the patient might be asked to cough.

At times, palpation immediately after the fracture might reveal a deformity produced by overriding of the displaced fragments.[7, 8, 10, 37] Later the callus may be palpable as a somewhat indistinct ridge; gradations from this finally include definite tumors as large perhaps as 2.5 by 2 cm. The discovery of crepitation, abnormal mobility, or callus is difficult when the broken ribs are covered with unusually thick soft parts, as in significant obesity or location under a large breast or under powerful muscles such as the pectoralis major and sacrospinalis. The patient should be in the optimum position for examination, that is, standing erect or in the dorsal decubitus. The seated position, especially in fat people, is the most disadvantageous.

The similarity between the pain of pleurisy and that caused by rib fracture has led to the diagnosis of many rib fractures as pleurisy. There are several reported cases, however, in which rib fracture led to pleural friction rub either from the fragments irritating the pleura or from localized hemorrhage. Hilton[74] reported the first such case. Wahl[134] reported 2 cases in which pleurisy developed at the fracture site. There was a suggillation the size of a Viennese thaler in Podrazki's[112] patient. The hemorrhage may be extensive as in the patient of Bodenheimer,[19] a man 67 years old, in whom the hemorrhagic spot over the fracture site was the size of the palm of the hand. The hemorrhage continued to spread until it involved the entire surface of the left half of the thigh. There was otherwise no bleeding tendency and the excised fracture site showed only perichondritis. Browning[27] reported the case of a patient with advanced tuberculosis who suffered from generalized

emphysema secondary to two rib fractures with displacement of the fragments following severe coughing. This seems to be quite rare after cough fractures but is well known to occur after trauma to the chest.[62, 88]

Roentgenography.—Occasionally, the roentgenogram shows definitely less density than normal, but usually there is no radiographic evidence of decrease of bone density. The ease with which early rib fractures might be overlooked in roentgenograms has been commented on repeatedly. The initial line of fracture is quite delicate, and because of the tendency for crowding of the ribs laterally, fractures in this zone may be missed. At times when callus has formed, reviewing of the earlier films may disclose the initially undiscovered break.

The need for oblique views was stressed by Mitchell[99]: of 14 fractures, 8 were seen only in the oblique views. However, Wynn-Williams[139] was unable to find fractures in lateral or oblique views which were not obvious in the anteroposterior position. It is our belief that not only should oblique views be taken but the film should also be exposed for bone detail (including use of Bucky diaphragm) rather than for soft tissue information, as is usually done in views of the chest.

CASE REPORTS

CASE 1 (Rib fracture simulating pleurisy).—Mrs. W. R., white, 55 years of age, had suffered from bronchial asthma since childhood. Within three or four days after development of an infection of the upper respiratory tract, moderately severe asthma associated with a persistent nonproductive cough appeared. Several days later she complained of intense pain over the right hemithorax anteriorly in the region of the seventh and eighth ribs which was aggravated by deep inspiration and particularly by coughing. Physical examination disclosed sibilant râles but no friction rub. It was thought that the patient had pleurisy, but a roentgenogram revealed definite linear fractures in the eighth and ninth ribs in the anterior axillary line on the right side.

CASE 2 (Rib fracture simulating angina).—D. G. R., a white attorney, 54 years of age, had suffered from "asthma" for the past two years. The asthma never awakened him at night. He had an intermittent nonproductive cough and exertional dyspnea which was worse shortly after arising. While playing golf one afternoon he had a paroxysm of coughing almost simultaneously with teeing off the ball. This was followed by severe precordial pain, radiating to the left shoulder and left hypochondrium, and severe dyspnea. He was barely able, with the help of friends, to return to the clubhouse. The pain persisted and was accompanied by some nausea. His physician had him hospitalized for the exclusion of a myocardial infarction. Numerous electrocardiograms were within normal bounds, and after two weeks' observation he was discharged. Roentgenogram of the chest had not been made. One week later, examination at the Ochsner Clinic disclosed obstructive emphysema plus callous formation over the fifth left rib near the costochondral junction.

CASE 3 (Rib fractures confused with metastatic carcinoma fractures).—Mrs. W. M. Y., a white housewife 43 years old, had had a left mammectomy elsewhere because of possible carcinoma of the breast. She had an attack of unrelieved coughing followed by generalized thoracic pain. A roentgenogram of the chest revealed slight accentuation of the pulmonary markings at the right base and multiple fractures involving the sixth and eleventh right ribs and the sixth through the eleventh on the left side with faint rarefaction of the bone on the region of several of these. In view of the multiplicity of the fractures with slight rarefaction and absence of trauma, these were considered to represent pathologic fractures secondary to metastases. Rib marrow aspiration disclosed no abnormality. Rib biopsy was

performed. The periosteum over the ninth rib was incised after palpation had failed to disclose the fracture site. A rather fresh fracture was found; the rib was cleaned off and this segment excised. Microscopic examination revealed essentially normal rib, marrow, and early callus. No metastatic tumor was present.

DIAGNOSIS

The diagnosis of rib fracture may be obvious, or not even suspected. Rarely does one think of a fractured rib if there has been no fall or blow to the chest or if the patient has heard no sound of fracture or felt anything give way. Sudden pain in a circumscribed region of the thoracic wall following cough is a daily occurrence; it is frequently a sign of minimal muscle damage or pleural irritation, and therefore one may easily pass over a fracture and attribute the pain to much more frequent occurrences of this sort. The ease of dismissing these lesions is illustrated by Tunis'[132] (1890) patient, who felt something snap in her side following a cough. "Not believing it possible she could have fractured a rib in this fashion, I gave her a sedative cough mixture and told her to apply a turpentine stupe. The next day she was complaining bitterly so *she was then examined* and a definite fracture discovered." (Italics mine.)

The clinical manifestations of rib fracture may be indistinguishable from pleurisy, in which case the diagnosis must be established roentgenologically. At times intermittent thoracic pain, often diagnosed pleurodynia, may precede the onset of pleural effusion by three to six months; in such cases the radiograph is usually normal. This was true in 10 per cent of 200 cases of tuberculous pleurisy with effusion studied by Sibley.[122] In epidemic pleurodynia there is usually no difficulty in making the diagnosis, for the triad of pain, fever, and headache is pathognomonic. According to Locke and Farnsworth,[86] the pain varies from mild pressure or discomfort to the extreme degree described as having an intense cutting or knifelike quality; in its severe form it may be paroxysmal and quite overwhelming. Locke and Farnsworth added other characterisitc features of the pain: (1) It is directly related to sneezing, laughing, coughing, deep breathing, and especially exercise. (2) Commonly the victim is leaning over a table or chair in a fixed position, or sitting or lying in a relaxed state. If relieved in this manner, motion of any sort is likely to precipitate a paroxysm of pain. (3) The patient walks slowly and deliberately, bent over with the body held rigidly. (4) Referred pain may be located anywhere on the trunk but the commonest sites are along the lower or lateral portion of the abdomen or chest in areas about three inches in diameter. (5) In the epidemic studied by Locke and Farnsworth the onset of fever was coincident with the pain and showed a sharp rise to a maximum of 104° or 105° in very severe cases. Prostration is at times extreme, but most cases subside promptly.

Pre-eruptive herpes zoster of one of the intercostal nerves may also present a clinical picture indistinguishable from pleurisy or rib fracture. With the appearance of vesicles, the differentiation becomes obvious.

Bone changes not produced by muscle action but rather by systemic disease must also be borne in mind when rib fractures are discovered on roentgenography. There is a large number of conditions in which pseudofractures mimic true breaks in bone. Camp and McCullough[29] listed the following conditions in which transverse zones of rarefaction may appear in various bones including the ribs: osteomalacia, rickets and late rickets, renal rickets, celiac disease, chronic idiopathic steatorrhea, Gee's disease, nontropical sprue, sprue, early and late osteogenesis imperfecta, fragilitas ossium, hyperparathyroidism, hyperthroidism, osteitis deformans or Paget's disease, adrenal-pituitary bone dystrophy, severe chronic acidosis or hyperglycemia, congenital syphilis, osteomyelitis, osteopetrosis (marble bones, osteosclerosis fragilis generalisata), states of overloading of bone (march fracture, insufficiency fracture), and certain blood dyscrasias. In referring to this list Albright, Burnett, Parson, Reifenstein, and Roos[5] pointed out that the bone disturbance in the first eight of these conditions is rickets or osteomalacia, depending on the age of the patient, and that the disturbance in the next two may be osteomalacia or rickets. They believed that "the ribbon-like zones of decalcification which occur in otherwise normal appearing bone, which last for months or years without regressing, and which exhibit a marked tendency to be symmetrical, occur only in osteomalacia or rickets." Looser[87] first described these under the term "Umbauzonen" (zones of transformation) in an extensive essay which appeared in 1920.

Milkman's syndrome derives from a carefully studied case first reported under the title "Pseudofractures" (1930); a second report entitled "Multiple Spontaneous Idiopathic Symmetrical Fractures" appeared in 1934 after the death of the patient. This patient exhibited "fractures" of the ribs as well as other bones. Although Albright and co-workers[5] established the identity of this condition as a variant of osteomalacia, they believed it should be retained as a separate entity because of the coexistence of pseudofractures and a skeleton which otherwise is not definitely abnormal as judged by roentgenograms. LeMay and Blunt[85] demonstrated that one factor determining the location of pseudofractures in osteomalacia is the position of the main arteries which lie on the bones. In their patients with rib lesions, it is surmised that these were at the site of branches of the intercostals; vessels were found in these areas in one of three cadavers examined by them.

Another "new" syndrome closely related, in the opinion of its discoverers Guichard and Lehmann,[66] to Milkman-Looser syndrome, has recently (1952) been reported under the name of costal fissures in chronic pulmonary disease. The reproduced roentgenograms certainly resemble those of rib fractures produced by cough; no indication is given of the status of the blood calcium, phosphorus, or alkaline serum phosphatase which would be useful in differentiating osteomalacia, osteoporosis, and osteitis fibrosa generalisata. Since there were no other bone anomalies than those noted in the ribs, it is believed that there is no validity for considering this syndrome as a separate entity.

Rib fractures have been considered to be malignancies either from the roentgenographic appearance or on physical examination. Wynn-Williams[139] remarked that if the rounded area of callus lies over the pulmonary field, it may be taken for an intrapulmonary shadow more easily than is generally realized. He saw two instances in which a callus around a rib fracture was temporarily diagnosed disease in the lung. I know of a patient who narrowly escaped operation for a cough fracture initially diagnosed malignancy. Case 3 (Mrs. W. M. Y.) had had a breast removed for suspected carcinoma. Because of slowly growing, slightly painful masses over the osteochondral junction of the second or third ribs, four patients were referred to Matthes and Thelen[93] with diagnosis of chondroma, sarcoma, osteochondritis, or tuberculosis. They were men between 20 and 35 years of age in good health with rather delicate bony structure but powerfully built musculature. Physical examination revealed a clearly visible mass ranging from the size of a pigeon's egg to that of a plum, and extending perhaps 0.5 cm. above the surface of the chest; it was in firm union with the rib, of the consistency of cartilage, and unattached to the overlying skin. On palpation the masses were slightly painful. Biopsy in 2 patients disclosed callous formation. In all 4 patients, questioning revealed that the fractures were probably caused by excessive physical exertion.

PROGNOSIS

The outlook in rib fractures is favorable for complete recovery with rich callus binding the rib ends together. In many cases the callus appears exuberant, especially with anterior or lateral fractures, probably because of the greater movement of this portion of the costal arch and hence the greater irritative stimulus exercised on the periosteum.[119] These fractures are rarely followed by any of the numerous complications of traumatic fractures of the ribs.[16] There are isolated reports of pseudoarthrosis (Wahl's[134] patient had pseudoarthrosis involving four ribs), of hemoptysis,[33] of extensive emphysema,[27] and of subcutaneous hemorrhage.[19, 112]

TREATMENT

The standard treatment for fractured ribs is strapping with adhesive. Blades[17] advised encirclement of the lower costal margin with a single four-inch strip of adhesive plaster regardless of the level of the fracture. The strapping should remain in place for at least three weeks. Christopher[35] recommended application of a tight circular muslin bandage around the entire chest; it gives much relief, does not irritate the skin, and can be changed easily and painlessly. Harmon[69] found that the use of a local anesthetic with prolonged action (eucupine hydrochloride) eliminated the necessity of strapping the thoracic wall and of excessive use of sedatives.

SUMMARY AND CONCLUSIONS

Rib fractures due to muscular action are not uncommon; in patients with infections of the respiratory tract the incidence of such fractures ranged be-

tween 0.08 and 6.5 per cent. The first instance of rib fracture from coughing was reported by Gooch[61] in 1773.

Muscular effort induced by coughing, sneezing, laughter, vomiting, straining at stool, or parturition may lead to broken ribs. Women are somewhat more prone to such accidents than men, approximately in a 3:2 ratio. Although these fractures occur at all ages, they occur most commonly in persons between 20 and 50 years of age. There are reports of 24 of these accidents in pregnancy; all occurred in the last trimester but only two occurred during labor.

Cough fractures have been reported in every rib but are quite rare in the uppermost and lowermost ribs. The first rib is, however, frequently the site of fracture from muscle stress unrelated to cough. Most fractures are found in the fifth through the tenth ribs, with a moderate preference for the left side. Ninety-three per cent of the reported cases were unilateral, and in 102 of the 142 reported instances only a single rib was involved.

The symptomatology or rib fractures produced by muscular action does not differ from that produced by trauma. At the moment of the accident, patients may feel something break or give way in the side; some fractures have been accompanied by a cracking sound. Pain is often intense and worsened by movements of the thorax.

Crepitation is common, and at times deformity may be palpated. The fractures are easily overlooked in the roentgenograms, especially if these are made before callus has formed.

The diagnosis may be simple, or not even suspected. The clinical manifestations may be indistinguishable from pleurisy; epidemic pleurodynia and preeruptive herpes zoster also have features in common. Rib fractures should also be distinguished from the pseudofractures seen in osteomalacia and other states. Rib fractures have at times been considered malignancies.

In those instances in which fractures produced by muscular action have been examined pathologically, essentially normal features have been revealed.

A structural analysis was made of the sixth rib using engineering principles to study the relative importance of various stresses. It was concluded that the incidence of fractures is greatest where bending stresses are greatest and shearing stresses least, and contrariwise, fractures occur least often where shearing stresses are greatest. Many rib fractures are probably the result of stress concentration and progressive cracking. Fractures may rarely be produced by sudden muscular contractions that are repeated at a frequency which corresponds to the natural frequency of vibration of the rib.

The outlook is favorable for complete recovery. Treatment consists in immobilization and/or local anesthesia.

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Surgical History

CONDUCTED BY JOHN R. PAINE, M.D.

EPONYMIC FRACTURES: ABRAHAM COLLES AND COLLES' FRACTURE

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. . . for be assured, that no man can know his own profession perfectly who knows nothing else.[4]

ABRAHAM COLLES (1773-1843) was the greatest of the Irish surgeons. He excelled as a clinician, as a teacher, and as an anatomist. His eponym is attached to a fascia, a space, a ligament, a law, and to a fracture. These suffice to keep his name alive, but in no way illuminate his great contribution to the surgical art.

THE FRACTURE

Colles had the good fortune to describe the most common fracture occurring in practice. As a result, his eponym is one of the most widely known and used. Although he himself was unaware of their reports, the French surgeons Pouteau (1725-1775)[8] and Desault (1744-1795)[6] had made previous mention of this fracture of the distal end of the radius. Colles' description appeared in 1814, and it has been recognized as a classic of brevity and clarity.[2] Unfortunately, this description is unaccompanied by an illustration, and surprisingly enough in view of Colles' reputation as an anatomist, there was no description of the dissection of such an injury. Perhaps this accounts for the fact that Colles placed the fracture so far proximally.

> This fracture takes place at about an inch and a half above the carpal extremity of the radius, and exhibits the following appearances.
>
> The posterior surface of the limb presents a considerable deformity; for a depression is seen in the forearm, about an inch and a half above the end of this bone, while a considerable swelling occupies the wrist and the metacarpus. Indeed the carpus and base of the metacarpus appear to be thrown backward so much as on first view to excite a suspicion that the carpus has been dislocated forward.
>
> On viewing the anterior surface of the limb, we observe a considerable fulness, as if caused by the flexor tendons being thrown forwards. The fulness extends upwards to about one-third of the length of the forearm, and terminates below at the upper edge of the annular ligament of the wrist. The extremity of the ulna is seen projecting towards the palm and inner edge of the limb; the degree, however, in which this projection takes place, is different in different instances.

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> The hard swelling which appears on the back of the hand, is caused by the carpal surface of the radius being directed slightly backwards instead of looking directly downwards. The broken extremity of the radius being thus drawn backwards, causes the ulna to appear prominent toward the palmar surface, while it is possibly thrown more towards the inner or ulnar side of the limb, by the upper end of the fragment of the radius pressing against it in that direction.[2]

Dissections of these fractures, such as those illustrated by Malgaigne,[8] and the use of x-ray pictures have resulted in a clearer concept of these fractures.

A Colles' fracture is a transverse fracture of the distal end of the radius, usually occurring within one inch of the articular surface. The articular surface of the distal fragment is tipped dorsally with the loss of its normal slightly volar inclination. The fracture may be accompanied by an avulsion of the styloid process of the ulna. There may be some comminution of the distal fragment with longitudinal fissures extending to the joint surface. These are rarely displaced. Such cases should not be confused with Barton's fracture-

Fig. 1.—Abraham Colles (1773-1843).

dislocation of the wrist.[11] Regardless of the methods of treatment employed, the functional end result following Colles' fracture are generally good, a fact recognized by Colles himself.[9]

THE MAN

Colles was born in Kilkenny, Ireland, in 1773. His father died when Abraham was 6 years old, and he was raised by his mother, who saw to his early education. In 1790, accompanied by his older brother, he entered Trinity Col-

lege, Dublin. One biographer remarks that while the older brother took the academic laurels, Abraham aimed at success in life rather than success in college.[10] During this period, Colles was apprenticed to Dr. Woodroffe, resident surgeon at Steevens' Hospital. Having gained his license from the Royal College of Surgeons in Ireland in 1795, he proceeded directly to Edinburgh for further study. Always an indefatigable worker, he notes in a letter home:

> As for my landlady, Mrs. Williams, she is positively afraid I shall read myself into a coffin, and actually comes to keep me idle at different times, out of her desire to keep me in health.[10]

After two years of further training, he was granted the degree of Doctor of Medicine.

Colles then set off for London, a distance of 400 miles, which he covered in only eight days. He had not been in London long before he fell under the spell of Astley Cooper. Cooper enlisted his aid in the preparation of some of the dissections for Cooper's monumental work on hernia, then in preparation. Plates of some of these dissections have recently been republished.[1] Colles' ligament, a portion of the aponeurosis of the external oblique muscle extending from Poupart's ligament to the linea alba, attests to his early interest in anatomy.

On his return to Dublin in 1797, while waiting for his practice to become established, Colles attached himself to a free dispensary maintained by the Quakers, and had an appointment as District Visitor to the Sick and Indigent Roomkeepers' Society. Two years later he succeeded his former chief, Dr. Woodroffe, as Resident Surgeon at Steevens' Hospital. At the age of 26 years, he had complete charge of one-third of the surgical beds in one of Ireland's leading hospitals.[7] Abraham Colles had arrived on the surgical scene. In 1802, he was elected President of the Royal College of Surgeons in Ireland, and two years later became Professor of Surgery, a post he filled with distinction for thirty-two years.

Toward the end of his career, he was passed over because of his life-long political views when the British Government sought to honor the leading figure in Irish medicine, a distinction uniquely Colles'. Public indignation over the slight caused the government to reconsider, and Colles was offered a baronetcy. He firmly, but modestly, declined.

> Mr. Colles won his way to eminence by means which are, to some extent, within the reach of all. He may be said to have wrested success from the hands of adverse fortune by his energy and indomitable perseverance. His family and decendants may point with pride to the unadorned name of Abraham Colles, and boast that they are sprung from one who merited a title, but declined it.[10]

THE ANATOMIST

> The subject of anatomy too generally ends at that point where it begins to be useful.[4]

Anatomy at the beginning of the Nineteenth Century was still taught on the basis of systems. The bones, the muscles, the nervous system, the vascular

system were all taken up in succession and dissected individually without any attempt to correlate them with the human fabric as a whole. As a result, the student might know the structures which cross the antecubital space but be totally unaware of their relationship to one another. It can be readily appreciated that such incomplete understanding had no value in the practical application of anatomy at the operating table. Colles was one of the first to recognize the need for the study of topographic anatomy with emphasis on the relationship between important structures in an area. His *Treatise on Surgical Anatomy*[4] published in 1811 introduced a new era in the teaching of anatomy.

> . . . while systems of anatomy are multiplied beyond number, we have scarcely any elementary treatises, the sole object of which is, to describe the relative position of the parts, or to point out the subserviency of anatomical knowledge to surgical practice. To supply that defect for the pupils of this school, is the design of the present work.
>
> The plans for the dissections have been laid down in such a manner as will enable the student to enjoy, from the dissection of each part of a single subject, a connected and comprehensive view of the structure: so that he may have it in his power to form an accurate idea of the various relations which the structure of this part bears to the phenomena of its diseases, and the modes of operation recommended for their removal.[4]

The book is literally a dissecting manual with a commentary on the surgical application of the anatomic relationships exposed. Its character is best illustrated by the perusal of Colles' description of what is now known as Colles' fascia.

> Now proceed to dissect the perinaeum. Raise the skin of the perinaeum, extending the dissection beyond the tubera ischii to the thighs. This exposes to view a strong fascia, which, on dissection, will be found to cover the entire of the perinaeum, and to blend itself with the structure of the scrotum. This fascia, although on a superficial view it appears continuous with the fascia of the muscles of the thigh, will yet be found, on closer examination, to attach itself very firmly to the rami of the ischium and pubes. The texture and connections of this fascia will serve to explain many of those phenomena attendant on the effusion of urine into the perinaeum, by rupture or ulceration of the posterior part of the canal of the urethra.
>
> First, then, you will find that this fluid, when so effused, although it forms a tumor in perinaeo, rarely terminates by suppuration and ulceration in this spot; being here resisted by the dense and unyielding texture of the fascia, diffusion laterally towards the thighs is prevented by the close attachment of this fascia to the rami of the pubes and ischium; while its progress forwards if favoured by a quantity of cellular substance, interposed between the surface of the perinaeal muscles and this fascia. In general, then, we find that the urine having caused some tumefaction in perinaeo, passes on into the scrotum. Here meeting with only a very feeble resistance from the lax texture of this part, it quickly distends it to a very considerable size. In some instances the mischief does not extend further, for suppuration takes place in the scrotum, and a quantity of very foetid fluid, composed of urine and pus, is discharged as soon as the abscess spontaneously bursts, or is opened by the surgeon. In other cases, the effused urine continues its progress until it arrives at the pubes.[4]

THE TEACHER

Among his contemporaries Colles was widely known for his ability as a teacher and lecturer.[12] His lectures on surgery were attended by as many as 300 students. He spoke fluently and relieved the tedium of his subject with the interspersion of practical anecdotes, sharply contrasting figures of speech, and an occasional *double entendre*. He was the outstanding attraction on the teaching staff, and largely as a result of his teaching the College attained the highest enrollment of any medical school in Britain during his tenure as Professor of Surgery. At the time of his retirement in 1836, the Royal College of Surgeons in Ireland passed a resolution stating:

> . . . it was the unanimous feeling of the College that the exemplary and efficient manner in which he had fulfilled the chair of the Theory and Practice of Surgery, for thirty-two years, had been the principal cause of the success and consequent high character of the school of Surgery in this Country.[12]

Colles had advanced ideas on medical education. His address to the pupils of the Royal College of Surgeons in Ireland, "On the Preparatory Education Necessary for the Surgical Student,"[4] should be required reading for deans and medical educators. He begins with a strong endorsement of a classical education and emphasizes the need for a knowledge of foreign languages.

> [Mathematics] No science tends so effectually to strengthen the understanding, and to improve the reasoning faculties, as that of mathematics; for it requires that complete retirement of the mind within itself, that straight-forward, unbroken progress of thought, which can alone enable us to follow up a long chain of arguments, and arrive at a remote conclusion. But besides the important benefits which are thus derived from the cultivation of this science, it is also in a great degree the key to most of the other sciences.
>
> [Natural philosophy] Natural philosophy will be found of great use to explain some of the functions of the animal body, and the laws to which they are subject. Thus it is impossible that any person unacquainted with the general principles of optics can form an accurate idea of the manner in which vision is performed in the natural state of the eye, and he consequently cannot clearly comprehend why distinct vision is in some persons confined to objects close to the organ while in others, those objects only which are placed at a distance can be seen distinctly.
>
> [Chemistry] Chemistry, Gentlemen, affords such a luminous explanation of the great phenomena of nature, and leads to such important improvements in the various arts subservient to human life that mankind at large must regard it as a science at once most highly pleasing, and most eminently useful. *To the surgical student in particular*, it is of indispensable importance. [Italics mine.]
>
> [Physiology] Physiology, which comprises a knowledge of the living actions of individual parts, and of the various functions of the animal system in a state of health, must obviously strike you, as being of essential importance to the surgeon. For without a knowledge of the healthy actions and functions, how can he know which of them are disturbed by disease? How can he undertake to regulate them when out of order? *Study them not in books, but in nature.* [Italics mine.]
>
> [Anatomy: To Colles, the study of anatomy was the foundation stone of the surgical education. He spent all of his life increasing the effectiveness of the teaching of this, his favorite subject.]

The stress on the basic sciences in the education of surgeons, which we like to think of as a recent trend, was nothing new to Colles, who justified it as follows:

> You may think, that if the time required for those general studies were devoted solely to the pursuits of your own particular profession, it would be more wisely and profitably employed. But his opinion is equally narrow and unfounded: for be assured, that no man can know his own profession perfectly who knows nothing else; and that he who aspires to eminence in any particular science, must first acquire the habit of philosophizing on matters of science in general.

Although limiting himself to a surgical practice, Colles had decided feelings in regard to the general medical education of the specialist.

> Since then it is absolutely necessary for the benefit and security of the patient, that the physician and surgeon should each be acquainted with both medical and surgical diseases, that surgeon must be inexcusable who is found to want this combined knowledge . . . Let it not be supposed that I would inculcate the idea of unnecessarily uniting the *practice* of both physic and surgery in the same person; on the contrary, I am decidedly of opinion, that in great cities the surgeon should never undertake the cure of a case purely medical, nor the physician of a case purely surgical. All I mean to assert is, that the *study* of both professions should be combined by the man who wished to practice either to the greatest advantage.[4]

In addition to writing about medical education, Colles took an active part in its reform and improvement. In 1828 he was responsible for establishing the chair of chemistry in the College, the first in any nonuniversity medical school.[12] The institution of chairs in medical jurisprudence, comparative anatomy, and botany also received his active support.

THE CLINICIAN

In 1837, late in his career, Colles published what he believed was his most important work, *Practical Observations on Venereal Disease and on the Use of Mercury*.[5] The dedication was to Sir Astley Cooper, his friend for over thirty-five years. In this work, Colles pitted his clinical acumen against that of John Hunter himself, and came off with the laurels. From the observation of cases in his practice, Colles demonstrated that, contrary to Hunter's opinion, the secondary lesions of syphilis can spread the contagion. Since they read the tragic case reports of women infected with syphilis by the examining fingers of their physicians, it is surprising that these clear-cut examples of disease transmission escaped the notice of both Semmelweis and Holmes in their search for evidence to support the theory of the contagiousness of puerperal sepsis.

Some of Colles' comments on the venereal diseases demonstrate his understanding of the human factor in disease, and also his sense of humor.

> I may be told by some that men may contract syphilis by sitting in a public privy; to this I can only answer that I have never witnessed a single instance; nor did the late Mr. Obre, who had been for many years most extensively engaged in treating the venereal disease; for on asking him if he believed that the disease was propagated in this manner, he shrewdly answered, that it sometimes was the manner in which *married* men contracted it, but *unmarried* men never caught it in this manner.[10]

In a masterful description of congenital syphilis, Colles traced the course of the disease from the child to the wet nurse, and then to the nurse's family. These observations form the basis of what is known as Colles' law, which is best stated in his own words.

> One fact well deserving our attention is this: that a child born of a mother who is without any obvious venereal symptoms, and which, without being exposed to any infection subsequent to its birth, shows this disease when a few weeks old; this child will infect the most healthy nurse, whether she suckle it or merely handle and dress it; and yet this child is never known to infect its own mother, even though she suckle it while it has venereal ulcers of the lip and tongue.[10]

It was observations such as this, based on a careful appraisal of a wide experience, which established Colles' reputation as a clinician.

CONCLUSION

In closing, Colles' ability as a surgeon should be mentioned. His description of the ligation of the subclavian artery is evidence enough of this.[3] His conception of the procedure was based on knowledge of the pathologic process; its execution was aided by his anatomic studies; the assessment of the end results was candid and critical. Here was a master surgeon who excelled as a teacher and writer. The ubiquity of his eponym is well deserved.

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Book Reviews

Pathology of the Fetus and the Newborn. By Edith L. Potter, M.D., Ph.D. Chicago, Ill., 1953, The Year Book Publishers, Inc.

The volume is not a functional pathology but a complete description of the normal variations in growth and development of the fetus and newborn infant, as well as the relation of the more extreme variations considered pathologic. The book is well organized into twenty-eight chapters, including weight and length tables for calculating the rate of antenatal growth and tables with the initial appearance of centers of ossification. There are 601 illustrations included and an important number of photomicrographs.

This book is a valuable addition to the library of the gynecologist and as a reference source for students and teachers.

The Principles of Neurological Surgery. By Loyal Davis, M.S., M.D., Ph.D., D.Sc. (Hon.), Professor of Surgery and Chairman of the Division of Surgery, Northwestern University Medical School, Chicago, Ill. Pp. 544, with 186 engravings, containing 354 illustrations and 5 plates, 4 in color. Philadelphia, 1953, Lea & Febiger.

The purpose of this book is to present the general principles of neurological surgery as applied to general diagnosis, therapy, and prognosis. A determined effort has been made by Dr. Davis to offer the material from the clinical viewpoint, and he has written it so that it may be a valuable book for referral by physicians engaged in general practice as well as those in special fields. It is comprehensive and includes a discussion of all the important neurological lesions. He has included the necessary neuroanatomic and neurophysiologic data required to understand properly the clinical development of the various lesions and methods of therapy. The first chapters include a thorough discussion of the techniques and significance of the neurological examination. Following this fundamental material, the various lesions of the nervous system are discussed. These include injuries, neoplasms, and inflammatory lesions of the skull, brain, spinal cord, and peripheral nerves. The remainder of the book includes material on the treatment of intractable pain, sympathetic nerve surgery, surgery of convulsive disorders, vascular malformations, anomalies, psychoses, and abnormal involuntary movements.

This fourth edition differs from the preceding editions in that many important additions and rearrangements have been made in the text. The material on peripheral nerve surgery has been entirely revised and rewritten to incorporate experiences obtained in World War II. The new diagnostic procedures, such as angiography for intracranial aneurysms and tumors, and radioactive isotope studies for localization of intracranial tumors, have been included. This greatly enhances the book as far as the majority of physicians are concerned.

This book has never been a particular reference work for specialists in neurological surgery, but has been directed more at those men in general practice, or in allied fields, who encounter neurological cases in the course of their practice. The emphasis has been on fundamental methods of diagnosis and prognosis, rather than on the outlining of specific operative procedures. The book is written, at times, with a confusing editorial style. This detracts from its usefulness but, in general, it is felt that it will be found to be a relatively authoritative source of ready information for most physicians. There are 354 illustrations, all of which seem to be well selected to demonstrate the desired data. The volume itself is on high-grade paper, and is excellently bound.

Clinical Orthopaedics, Vol. I and II. Edited by Anthony F. DePalma. Philadelphia, 1953, J. B. Lippincott Company.

The first two volumes of this new publication are now available, and from their contents the value of this series to the orthopedic scene can be fairly evaluated. In the prospectus, we read that this series will not be a "rehash" of material published elsewhere but will provide an outlet for valuable orthopedic investigations, material of scientific, practical, and academic value. Alas, this is not the case.

In Volume I, the first sentence of the first article, "Rheumatism is the leading cause of death in children," is obviously untrue. The second article describes the treatment of a normal anatomic variation with corrective braces and exercises. Fig. 73 illustrates an improper treatment for femoral shaft fractures mislabeled Bryant's traction. In this same section on femoral fractures, the writer states his preference for the Hansen-Street intramedullary nail rather than the Küntscher nail, "which bends or breaks in a great percentage of cases." This is not true. With incredible naïveté, the author of an article on "Trigger Thumb in Infants," after describing this operation in fourteen such cases, says, "The author, however, is at a loss to explain what happens to these youngsters if no treatment is given. . . . The inference is that some infants must have this condition and recover without benefit of treatment. . . ." Meddlesome surgery?

Volume II, devoted in a large part to the intramedullary nailing operation developed and popularized by Küntscher, fails even to mention his name in the historical introduction, a damnable omission. Of the remaining material on intramedullary nailing, hardly any is appearing for the first time. Indeed, a great deal of it has been published by the American Academy of Orthopaedic Surgeons.

The material in these volumes is not scientific, for there is not one article on the investigation of a basic problem of an orthopedic nature; it is not practical, unless overtreatment and meddlesome surgery can be considered practical; and it is hardly academic, as a glance at the bibliographic references will quickly reveal.

Morris' Human Anatomy. A Complete Systematic Treatise. Edited by J. P. Schaeffer. Ed. 11. Pp. 1718, with 1220 illustrations. New York and Toronto, 1953, The Blakiston Company.

The eleventh edition of *Morris' Anatomy* appears for the second time under the editorship of Dr. Schaeffer. All the contributors are Americans. The first edition appeared under the editorship of Sir Henry Morris, an English surgeon and anatomist. This reviewer came to know this anatomic text best under the editorship of the late distinguished anatomist, Dr. C. M. Jackson, who continued as editor of the fifth (1914) through the ninth editions (1933).

The present volume is a very readable book. The illustrations, many of which are in color, are considerably better than those in the earlier editions. And this consideration is one of great importance, not only to undergraduate students of medicine, but also to physicians and especially to surgeons, whose eyes, of necessity, must pore often and at frequent intervals over anatomic texts. It is to be hoped that medical students may some time enjoy the great privilege of studying anatomic texts profusely illustrated in color, as in some of the well-known German texts of an earlier day.

This volume should find favor with medical students as well as surgeons who want a ready, readable anatomic text with superior illustrations by well-known American anatomists.

The Year Book of General Surgery (1953-1954 Year Book Series). Edited by Evarts A. Graham, with a Section on Anesthesia edited by Stuart C. Cullen. Pp. 590. Chicago, 1953, The Year Book Publishers, Inc. $6.00.

The Year Book of Surgery, edited by the distinguished American surgeon Evarts A. Graham, continues to be a very interesting and instructive monograph. Some of the best

readings in the text are the mature comments made by the author. The tone of the volume is set in the Introduction written by Dr. Graham, which suggests very forcefully the nature of the change in surgery which has occurred in this country during the past three decades. That interesting foreword to the volume indicates the editor's attitude toward what constitutes modern surgery, and is reprinted here in full. The volume can be recommended enthusiastically as interesting reading which will hold the reader's attention.

"At the meeting of the International Surgical Society in New Orleans in 1949 one of the prominent older European members criticized the program to your editor. His chief complaint was, as he put it, there was too much chemistry and not enough surgery. The remark led to my query, what is surgery anyway? His answer revealed the fact that to him the surgery of today is very little different from that in the early days of this century. That is to say, surgery is an art dependent upon the application of anatomy and pathology to the job at hand. To him the advances made in the last half-century or so and those still to be made consist chiefly of new operations. He completely overlooked the great improvements in diagnosis, in postoperative care and in surgical mortalities which have occurred.

"This astonishing concept of our profession raised several questions in my mind. Does he not realize that there is a science as well as an art of surgery? Must we still think of it in the etymologic sense as the work of the hand? Does the surgeon not require also a brain? Surely we have advanced beyond the stage of being practitioners of external medicine as contrasted with those who practice internal medicine.

"To one who during his life has seen a change from a glorification of the art of surgery to a recognition of the importance of the scientific aspects, the criticism by my European friend came as an unbelievable expression of an opinion supposedly obsolete for many a year. During the period of glorification of the art of surgery, manual dexterity and rapidity of operating were criteria used in gauging the excellence of the surgeon. He who performed a greater number of operations per year was ordinarily considered a better surgeon than he who perhaps sought to be less busy in the operating room but to have more time for meditation, reading, research, of either a clinical or a laboratory nature, and, yes, even perhaps to learn something of a science that might contribute to the solution of some of his daily problems. The one-thousand-laparotomies-a-year man was the big shot, and on him most of the young surgeons looked with envy.

"The teaching of surgery in this country in those days was carried out by herding together in an amphitheater a crowd of medical students to watch the professor gallop through a string of operations with occasional remarks about what he was doing. That was about the only information which the students got, because they could see practically nothing of the field of operation. A big list of operations meant a big surgeon. Aspiring young surgeons learned their profession by acting as assistants to established surgeons if they were lucky enough to know men with whom they could work or, as more often occurred, they learned to operate by using the experimental method on such unsuspecting patients as were willing to allow the tyros to operate on them. It was a sort of catch-as-catch-can procedure. Catch the patient and learn operative technic on him.

"Now how different the whole situation is! Standards of judging surgeons have changed. Much of the glamor has gone. Facilities for obtaining a good training in surgery are abundant. The amphitheater operating clinics as a method of teaching surgery have become obsolete.

"My friend who was critical because he thought there was too much chemistry and not enough surgery on the program failed to recognize one of the most important contributions to surgery which Lister made. Of course, everybody knows that the introduction of the antiseptic method revolutionized the practice of surgery and greatly extended its field of application. But perhaps a greater revolution was a philosophic one which has never received the emphasis it deserves. Here was a young surgeon well versed in, but dissatisfied with, the current art of practice who saw the possibility of applying to surgery the work of a young chemist by the name of Pasteur who was working in a foreign land and publishing his results

in a foreign language. Could anything at that time have seemed less applicable to the practical art of surgery than a chemist's contributions to the philosophic problems of spontaneous generation, fermentation and putrefaction?

"Nowadays it is true that more and more young surgeons are calling upon chemistry and physics to assist in the study of surgical problems. This is as it should be. More power to them! Every cell is a chemical laboratory. Even as practical a matter as the healing of a wound is fundamentally a chemical phenomenon. Some day a new young Lister will come along and by applying chemistry to his studies will learn how to shorten the period of wound healing from a week or 10 days to 2 or 3 days. In the meantime, let the programs of the surgical societies and the surgical journals contain more rather than fewer papers dealing with the application of chemistry to surgical problems! Anyway, the Year Book is glad to publish abstracts of many of the papers of that kind, because they represent the surgery of 1953 and not that of 1900."

Conduction Anesthesia. By George P. Pitkin, M.D., edited by James L. Southworth, M.D., Robert A. Hingson, M.D., and Winifred M. Pitkin, M.D. Ed. 2. Pp. 1005, with 36 tables and 585 illustrations. Philadelphia, 1953, J. B. Lippincott Company.

A comprehensive and thorough revision and modernization of the original "encyclopedia" of regional anesthesia is offered in the second edition of *Conduction Anesthesia.*

The basic neuroanatomy section of the book has been enlarged by the inclusion of a chapter on the vertebral canal. Modern techniques such as transtracheal cocainization appear in the new chapter on topical anesthesia agents. Similarly, a chapter on the complications of conduction anesthesia, including their causes, preventions, and specific treatments, has been added.

Of even greater interest in the revision of the section on the pharmacology of local anesthetics, which places major emphasis on hypotension, the principal untoward action of these agents. Many obsolete compounds have been deleted, and such popular new compounds as Xylocaine have been added. The use of vasopressor drugs in conjunction with anesthetic agents is dealt with much more fully. Furthermore, the addition of new equipment (polyethylene and vinoplastic catheters) to the surgeons' and anesthesiologists' armamentarium is included.

The recent popularity of extradural anesthesia has necessitated the revision of the chapter on this subject. Alterations have been made in the section on spinal anesthesia so that it now contains the most modern spinal anesthetic techniques and agents. In addition, there is a topographic table of the relationships of the spinal nerves and attachments to the spinal cord and their vertebrae. An important supplement to the chapter on the anatomy of the spinal nerves concerns the dermatomes, myotomes, and scleratomes, with numerous diagrammatic illustrations. The anatomic section on the autonomic nervous system has been rewritten, and emphasis placed largely on various reflex arcs which are more fully described and illustrated. Included also are diagrammatic illustrations of the afferent and efferent innervation of the various organs by both the parasympathetic and sympathetic pathways. Another important addition is the section dealing with anatomic innervation of the adrenal glands. Moreover the section on local anesthesia now includes specific nerve block techniques for cesarean section and labor, and there has been much revision and enlargement of the section on therapeutic and diagnostic conduction anesthesia.

As in the first edition, this volume represents a complete encyclopedic treatment of nerve block anesthesia. The various sections dealing with specific nerve blocks are individually approached from an anatomic standpoint, even though this necessitates much repetition of the pertinent neuroanatomy involved. The techniques of the specific blocks themselves are described from every practical anatomic approach. This in itself makes the book unique since many patients have pathologic restrictions to what is perhaps the best approach, and it becomes necessary for the surgeon or anesthesiologist to choose some alternative approach.

Although this text is specifically intended for the anesthesiologist and the surgeon, it will prove of immeasurable benefit as a reference guide to the neurologist, the obstetrician and gynecologist, the ophthalmologist, and the dentist, as well.

Pathologie vasculaire, medicale et chirurgicale (Vascular Pathology, Medical and Surgical). By Marceau Servelle. Paris, 1952, Masson & Cie.

This book is essentially a text for the surgeon interested in clinical applied vascular surgery. It includes the practical approach to the various arterial, venous, and lymphatic problems and also includes the surgical treatment of the congenital cardiac anomalies, as well as those of the acquired type.

Written in French, it reads very easily, and the author presents reasonable arguments for his particular approach to the various vascular lesions. There are adequate illustrations to emphasize his statements. While the reference form is not that which the American medical reader is used to, the author does include some references in his historical accounts and discussions of the subject. However, no formal bibliography is presented.

In some areas, the author has gone a little further than the average vascular surgeon's interests, for example, in discussion of intracranial aneurysms and their treatment. In other areas, the discussion is usually brief, as in his short section on thoracic and abdominal aortic aneurysms. There are many errors that would have been picked up by more careful proofreading. (As examples of this, one can cite the misspelling of Raynaud which appears on page 38 as Reynaud. Also such errors as the author's reference on page 61 to Dr. E. Allen of the Mayo Clinic as a vascular surgeon.)

The advances being made in the field of vascular surgery are so rapid that a text such as this is outdated much more than the average textbook by the time it goes to print. The loose paper binding does not stand up well. A table of contents is given at the end of the book which is of some value, but it would seem that a text of this sort would deserve an index as well as a table of contents.

In summary, this French text presents in a fairly clear fashion some worth-while material for the clinical surgeon interested in vascular disorders of various types. The rapid advances which have been made recently in the field of vascular surgery make the author's experiences which are presented here somewhat more out of date than in the usual textbook.

Prostatectomy: A Method and Its Management. By Charles Wells, professor of surgery, University of Liverpool. Pp. 103, with 72 figures, 17 tables, and 65 references. Cloth. Chapters on history, pathology, sequellae, clinical features, indications for treatment, anesthesia, surgical technique, postoperative care, severe chronic urinary retention; fluids, electrolytes, and proteins; analysis of 205 consecutive admissions to hospital for prostatism, and late results. Edinburgh and London, 1952, E. & S. Livingstone.

Of the 205 patients in the series, 47 had acute and 56 high-grade chronic retention. The blood urea was normal in 84 and elevated in the remainder. Ninety were past 70 years of age. Ten had stones in the bladder, 10 had vesical diverticula, and 4 had papillomata. The surgical mortality was 3 per cent. While the catheter was removed on the fifth day, only 27 patients were discharged before the fourteenth day; the others stayed longer, many up to three or four weeks. Penicillin and a triple sulfonamide were used before operation, and Mandelamine afterward.

Follow-up was carried out for one to three years in 194 patients. None was incontinent of urine, and none had obstructive symptoms.

This book is a forthright discussion of the experience of the author and his associates with their version of the "aseptic" suprapubic enucleation of Wilson Hey. The novel aspects of this technique include avoidance of catheterization before operation, and the retrograde passage and fixation of a urethral catheter at its conclusion. Otherwise, the operation itself is a conventional suprapubic enucleation with careful hemostasis with diathermy, Oxycel, and Gelfoam.

The urinary tract is investigated beforehand only by excretory urography. Urinalysis and culture are carried out before operation only if the patient is able to void. Impaired renal function is not regarded as a contraindication to operation; indeed, 121 of the 205 patients had elevated blood ureas, some as high as 150 mg. per cent. In many instances, operation is performed as an emergency in patients with acute retention. Drainage with a catheter is employed only when serious extraurogenital lesions require treatment in patients with complete or nearly complete retention.

While this attitude toward preliminary drainage contravenes one of the most firmly established principles of modern urology, the author's results suggest that the old principles may be wrong. He states that no patient was refused operation; yet, the mortality was but 3 per cent in 205 consecutive cases! This leads one to wonder what could be achieved by applying the same principles to transurethral resection.

The reviewer does not share Mr. Wells's grim attitude toward catheterization, and has achieved a mortality in transurethral resection considerably lower than the author's in "aseptic prostatectomy," despite free use of the catheter. It is necessary to point out, too, that a mortality of 3 per cent in 205 cases does not mean that it would be the same in 1,000 such cases. That there may have been a certain element of luck in a surgical mortality of 3 per cent with this operation is suggested by Aiken's report (Brit. J. Urol. **25**: 20 [March] 1953) of fifteen deaths in 150 cases.

This book should be read by every surgeon who has occasion to operate upon the prostate gland. One who does so, and then reads the treatises of Millin on retropubic, of Nesbit and of Barnes on transurethral, and of Young on perineal prostatectomy will be very well informed about prostatectomy.

ANNOUNCEMENT

1953-1954 SCHOLARSHIPS IN PLASTIC AND RECONSTRUCTIVE SURGERY

The Foundation of the American Society of Plastic and Reconstructive Surgery announces the regulations of the Fifth Annual Scholarship Contest:

1. The contest in *Junior* Classification is restricted to residents in training and to plastic surgeons who have been in practice *no longer than five years.*
2. Two main prizes are offered, each consisting of a *three-month plastic surgery scholarship* with full maintenance in a number of selected leading services, in the United States and abroad.
3. The subject matter of the essay must be the result of some *original* research (either clinical or experimental) in the field of plastic and reconstructive surgery. The thesis should be of about 5,000 words, and written in English.
4. Work previously published wholly or in part is not acceptable.
5. Expenses of travel between the services will be allotted.
6. A silver plaque or a certificate of honorable mention is also offered for a winning essay in *Senior* Classification to contestants active in practice of plastic and reconstructive surgery for *more than five years.*
7. Manuscripts will not be accepted by the Award Committee *after July 1, 1954.*
8. The winning essays will be presented in person at a formal program of the Foundation of the A. S. of P. and R. S. to be held in the fall of 1954.

The 1953 Scholarships were awarded to Robert M. McCormack, M.D., Rochester, N. Y., for an essay, "Simultaneous Chordee Repair and Urethral Reconstruction for Hypospadias," and to James Calnan, F.R.C.S., Oxford, England, for an essay, "The Error of Gustav Passavant," subtitle: "A Refutation of the Recognized Velo-Pharyngeal Mechanism in Speech."

For further information, write to the Award Committe, c/o Jacques W. Maliniac, M.D., Chairman, 30 Central Park South, New York, N. Y.

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